DOCTOR OF PHILOSOPHY

Stroke Prevention Rehabilitation Intervention Trial of Exercise (SPRITE)

A Randomised Feasibility and Pilot Study

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Stroke Prevention Rehabilitation Intervention Trial of Exercise (SPRITE) –A Randomised Feasibility and Pilot Study

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Declaration

I hereby declare that:

a) This thesis is not one for which a degree has been conferred by this or any other University.

b) The work described in this thesis and its composition is my own work, carried out under the auspices of the Department of General Practice and Primary Care and the Centre for Public Health, Queen's University Belfast.

c) The work of this thesis has not been presented to any other institution.

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Summary

Introduction

The value of cardiac rehabilitation (CR) after a transient ischaemic attack (TIA) or 'minor' stroke is untested despite these conditions sharing similar pathology and risk factors to coronary heart disease.

Aims

To develop and test the feasibility of conducting a randomised controlled trial of a novel home-based rehabilitation programme, '*The Healthy Brain Rehabilitation Manual*', with a pedometer, for patients with a first TIA or 'minor' stroke of atherosclerotic origin, utilising the core components of home-based CR. This thesis describes the systematic reviews of the literature, qualitative research and feasibility and pilot studies of the intervention, developed according to the Medical Research Council (MRC) guidelines for developing complex health service interventions.

Method

Systematic literature reviews informed adaptation of a home-based CR manual. This was further refined through 3 focus groups (TIA/minor stroke patients and carers; clinical academics; and health professionals). Next, a 6 week feasibility study randomly allocated participants to 3 arms: (1) standard/usual care; (2) manual; (3) manual plus a pedometer. All groups received telephone follow-up at 1 and 4 weeks post-enrolment. Biophysical and questionnaire assessments at baseline and 6-weeks

included VO_{2max} testing. Two trained review authors independently assessed the manual to identify the Behaviour Change Techniques (BCTs) used.

For the 12 week pilot trial participants were randomly allocated to: (1) standard care (n=12); (2) manual plus pedometer with telephone follow-up by General Practitioner (GP) (n=14); (3) manual plus pedometer with telephone follow-up by stroke nurse (n=14). The telephone follow-up was undertaken at 1, 4 and 9 weeks. Focus groups were undertaken to explore participants' views on the intervention. Eligibility criteria for both the feasibility and pilot studies included being within 4 weeks of a first TIA or 'minor' stroke.

Results

a) Systematic review 1

Only 4 studies were identified which utilised lifestyle interventions within the first 90 days following a TIA and/or 'minor' stroke, highlighting the dearth of evidence of non-pharmacological interventions in this area. The main behaviour change techniques (BCTs) used within the included studies were goal setting and instructions about how to perform given behaviours.

b) Systematic review 2

I reviewed the BCTs utilised in home-based CR and published between 2005-2015. Twenty different BCTs were used in the 11 included studies, with social support (unspecified) used in all studies and goal setting (behaviour) in 10. Of the 11 studies, 10 reported effectiveness in reducing CVD risk factors.

c) Feasibility Study

Twenty-eight patients were invited to participate, with 15 (10 men, 5 women; 9 TIA, 6 minor stroke; mean age 69 years) consenting. Participants completed all assessment measures except VO_{2max} testing, which all declined. The intervention was viewed positively and pedometers valued highly, particularly for goal-setting. Overall, 36 BCTs were used in the intervention, commonest centred around goal setting, planning and social support.

d) Pilot Study

Of 125 eligible patients, 44(35.2%) consented to initial study contact, with 40(90.9%) participating and 39(97.5%) completing the study. From baseline to follow-up, there was a general improvement in cardiovascular risk factors in the intervention arms. Qualitative work with participants and stroke nurses confirmed acceptability of the research study and intervention with some amendments suggested.

Conclusions

It is feasible to conduct a trial to evaluate the effectiveness of a novel home-based CR programme, '*The Healthy Brain Rehabilitation Manual*', implemented within 4 weeks of a first TIA/minor stroke. This intervention has been developed following the MRC guidelines, with clear patient and public involvement, and has demonstrated improvements in cardiovascular risk factors. The commonest BCTs used within the manual revolve around goals, planning and social support. The findings from the feasibility and pilot work will be used to further refine the next stage of the

intervention's development, a randomised controlled trial, powered to detect reductions in systolic blood pressure.

Dedication

"Not everything that can be counted counts, and not everything that counts can be counted...

In the middle of difficulty lies opportunity"

Albert Einstein

"Today's rain is tomorrow's whisky."

Traditional Scottish proverb.

For Laura, Leo and Sofia.

Annie and Catherine……always in my thoughts and heart.

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Presentations

Heron, N; Kee, F; Cupples, ME; Tully, MA. **Should GPs target physical activity counseling for patients with long-standing illness or disability?** Oral presentation at AUDGPI, Belfast, March 2015.

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Heron, N; Kee, F; Cupples, ME; Tully, MA. **How can GPs better target the general population and those with a longstanding illness/disability for physical activity and sport participation counselling?** Oral presentation at the Annual Public Health Agency conference, Belfast, June 2015.

Heron, N; Prof F Kee; Dr MA Tully; Dr C Cardwell; Prof Donnelly; Prof ME Cupples. **Review of the Behaviour Change Techniques in Home-based Cardiac Rehabilitation Programmes.** Oral presentation at AUDGPI, Dublin, March 2016.

Heron, N; Prof F Kee; Dr MA Tully; Dr C Cardwell; Prof Donnelly; Prof ME Cupples. **Systematic review and meta-analysis of secondary prevention**

rehabilitation programmes initiated within 90 days of a TIA or 'minor' stroke. Elevator pitch oral presentation at SAPC, Dublin, July 2016.

Heron, N; Prof F Kee; Dr MA Tully; Dr C Cardwell; Prof Donnelly; Prof ME Cupples. **A Systematic Review and Meta-analysis of Rehabilitation Programmes with Secondary Prevention Lifestyle Interventions Initiated within 90 days following a TIA or 'minor' stroke.** Oral presentation at AUDGPI, Limerick, March 2017.

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Heron, N; Kee, F; Donnelly, M; Cupples, ME. **Systematic review of rehabilitation programmes initiated within 90 days of a transient ischaemic attack or 'minor' stroke: a protocol**. BMJ Open, 2015; 5: e007849. doi:10.1136/bmjopen-2015-007849.

Heron, N; Kee, F; Tully, MA; Donnelly, M; Cupples, ME. **Systematic review of the use of behaviour change techniques (BCTs) in home-based cardiac rehabilitation programmes for patients with cardiovascular disease – protocol.** Systematic reviews. 2015, 4:164. doi: 10.1186/s13643-015-0149-5. URL: http://www.systematicreviewsjournal.com/content/4/1/164

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Heron, N; Kee, F; Cardwell, C; Tully, MA; Donnelly, M; Cupples, ME. **Rehabilitation Programmes with Secondary Prevention Lifestyle Interventions Initiated within 90 days following a TIA or 'minor' stroke: Systematic Review and Meta-analysis.** British Journal of General Practice (BJGP). 2017 Jan;67(654):e57-e66. doi: 10.3399/bjgp16X688369.

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Heron, N; Kee, F; Mant, J; Reilly, P; Cupples, ME; Tully, MA; Donnelly, M. **Stroke Prevention Rehabilitation Intervention Trial of Exercise (SPRITE) - A Randomised Feasibility Study.** BMC Cardiovascular Disorders. Dec, 2017, **17**:290 https://doi.org/10.1186/s12872-017-0717-9

Awards and Achievements

- NIHR PhD Clinical Fellowship award, August 2014 – 2018.
- Elected faculty council member of the Faculty Sport and Exercise Medicine, FSEM (UK), 2015 - 2019.
- BASEM Fellowship & Doctoral Level Research in Sport & Exercise Medicine Bursary award, April 2016 – 2018.
- Highly commended abstract for the Northern Ireland Stroke Forum annual conference, June 2017.

Abbreviations and Definitions

- BCTs – behaviour change techniques
- BMI – body mass index
- BP – blood pressure
- CI – confidence intervals
- CR – cardiac rehabilitation
- CT scan – Computed tomography scan
- EQ-5D-5L – EuroQuol group questionnaire; standardized instrument used to measure health outcomes providing a single index value for health status.
- GP – General Practice or General Practitioner
- HADs – Hospital Anxiety and Depression scale
- HR – heart rate, expressed in beats per minute
- IPAQ – International Physical Activity Questionnaire
- MCID – Minimally Clinically Important Difference
- MDM – Multiple Deprivation Measure
- METs – metabolic equivalents
- MI - myocardial infarction
- MRC – Medical Research Council
- MRI – Magnetic Resonance Imaging
- NI – Northern Ireland
- NICE – National Institute of Health and Care Excellence
- PASE - Physical Activity Scale for the Elderly
- SAPAS – (Northern Ireland) Sport and Physical Activity Survey
- 6MWT – Six minute walk test
- TIA – transient ischaemic attack

- TUGT – timed up-and-go test
- 2MWT – Two minute walk test
- UK – United Kingdom
- WHO – World Health Organisation

Preface

The research contained in this thesis was performed during my 4 years as a NIHR Clinical Academic PhD Fellow (September 2014 – September 2018).

I first became interested in rehabilitation and secondary cardiovascular prevention through my own athletic participation, my first passion being football, as well as through my clinical work within sport and exercise medicine and primary care. This interest was further supported by a BSc (Hons) intercalated degree in the area of sports medicine and a MPhil research degree which assessed physical activity promotion within primary care as well as a Masters in Public Health, in which I conducted a review of the factors associated with sport participation in adults with long-term disability.

Throughout my medical career I have always seen physical activity promotion and, more widely, secondary cardiovascular prevention as imperative, especially when the contribution of non-communicable diseases to the burden of chronic diseases are considered. In my role as General Practitioner (GP), particularly in an area of high deprivation, I feel it is particularly important to educate all patients with regards cardiovascular prevention and I particularly enjoy advising patients about how to become more physically active. Health professionals in this area often neglect health promotion due to the time constraints placed on GPs and the perceived lack of knowledge. Yet we know that certain patient groups, particularly those that have suffered cerebrovascular events, are at significant risk of future cardiovascular events, which will then have a significant impact on them personally, their families and wider society. An important area of research is therefore the feasibility of conducting secondary prevention following an initial cardiovascular event such as a transient

ischaemic attack (TIA) or ‘minor’ stroke. Indeed stroke, a major cause of death and disability may be prevented by intervention following a TIA or ‘minor stroke’ but the best approach to such prevention remains unknown. Through this study I therefore wanted to develop a home-based intervention, using core components of cardiac rehabilitation, with or without an added pedometer intervention, to promote secondary cardiovascular prevention in this patient group.

Chapter 1 describes a review of the current literature in terms of TIAs, minor stroke and secondary cardiovascular prevention. In Chapters 2 and 3, systematic reviews of the literature are presented in terms of secondary prevention lifestyle interventions initiated within 90 days of a TIA/minor stroke and the behaviour change techniques (BCTs) used within home-based cardiac rehabilitation programmes. Chapter 4 then presents the initial qualitative work done on the proposed intervention, ‘*The Healthy Brain Rehabilitation Manual*’, with Chapters 5 and 6 then presenting the feasibility and pilot studies conducted on this intervention. Finally, Chapter 7 then provides an overall summary to the thesis.

My aim is that by the end of this PhD, clinicians and health professionals will have an appropriately evidence-based intervention to promote secondary prevention to those who have just suffered a TIA and ‘minor’ stroke and that this intervention will satisfy the current unmet needs in this patient group as well as reducing their future risk of cardiovascular events. My hope would now be that I could apply for further funding to continue to develop this intervention and a randomised controlled trial to prove its effectiveness in reducing further vascular events when implemented immediately post-TIA and minor stroke.

Chapter 1

- Literature Review

TIA and 'Minor' Stroke and the Secondary Prevention of Stroke

1.1 Stroke prevalence, impact and risk assessment

Strokes and transient ischaemic attacks (TIAs) are highly prevalent conditions. Stroke killed 5.7 million people worldwide in 2005 and was estimated to cause 6.5 million deaths in 2015 (1), with stroke survivors often being left with considerable disability (2) and indeed, stroke is the leading cause of disability within the United Kingdom (UK) (3). At least 57,000 new strokes occur each year in England, with 32,000 stroke-related deaths reported each year (4). Approximately a quarter of people who experience a stroke will leave hospital with a moderate or severe disability (4) and, while stroke incidence increases with age, 38.2% are reported to occur in people aged between 40-69 years of age (4). Indeed the average age of a first stroke is gradually falling (4), currently reported to be 68.2 years of age for men and 73 years of age for women (4).

In 2016, 36,741 patients were living with stroke in Northern Ireland (NI) (5) and in 2006, approximately 1,700 TIAs and 4,000 strokes occurred in NI alone (6). Many strokes are preceded by TIAs in the previous ninety days (7), and therefore the immediate period after a TIA is a crucial time to intervene to reduce the risk of stroke.

The 90 day risk of vascular events following a TIA or 'minor' stroke, excluding events within the first week after diagnosis when the risk is highest, can be as high as 18% (8), a figure supported by other studies (9). The $ABCD^2$ score (derived from a calculation based on the individual's age, blood pressure, clinical signs, duration and diabetes - see Section 2.2 for further details) in patients with a TIA is used to identify the future risk of stroke (7). The presence of a new infarct, identified on brain imaging

and indicating that the patient has actually had a stroke rather than a TIA, places the patient at higher risk of a further stroke within the first 90 days (10).

1.2 **Stroke prevention**

Immediate assessment of TIA and 'minor' stroke patients following the initial event, with initiation of secondary prevention focused on pharmacological interventions, can reduce the 90 day risk of stroke to 2% within the research setting (11). Indeed Rothwell et al (11) conducted a prospective study on 1,278 patients in Oxford, United Kingdom (UK), with a TIA and/or stroke and followed them up for ninety days. They found that the 90 day risk of recurrent stroke in the patients referred to the study clinic reduced from 10·3% to 2·1% when assessment and treatment was initiated within, generally, twenty four hours of the initial event. This is particularly true for initiation of aspirin therapy (12). These results have however not been replicated within routine practice, with most patients waiting at least a week from the incident event before being reviewed by a specialist and secondary prevention mechanisms introduced (13), despite recently released guidelines advising review of TIA symptoms within 24 hours in a specialist neurovascular clinic (14).

Evidence is growing regarding the contribution of change in modifiable risk factors to reductions in cardiovascular deaths (15) and there is a need to consider how to promote non-pharmacological measures within secondary prevention (16). Indeed Hughes et al (15) found that approximately 60% of the reduction in coronary heart disease, which shares a similar underlying pathological mechanism to cerebrovascular disease, in NI between 1987 and 2007 was due to changes in modifiable cardiovascular risk factors and only approximately 35% of the reduction was

attributable to medical or surgical treatments.

2. Transient Ischaemic Attack (TIA) and 'minor' stroke

2.1 Definition of TIA and minor stroke

TIA and 'minor' stroke are defined clinically by the patient's history, a neurological examination and neuroimaging (typically a CT and/or MRI head scan), with evidence of infarction indicating a diagnosis of stroke and the absence of infarction indicating TIA (17). Typical symptoms of a TIA and stroke include the rapid onset of speech disturbance, unilateral weakness or sensory loss, monocular blindness, visual field defect or ataxia, amongst others. TIA is defined as "a transient episode of neurological dysfunction caused by focal brain, spinal cord or retinal ischaemia, without acute infarction" (10). Whilst stroke has traditionally been defined as "an acute onset of focal neurological symptoms which last more than twenty-four hours" (18), a more up-to-date definition is "the acute onset of focal neurological symptoms from the brain, retina or spinal cord of any duration, in which imaging or autopsy show focal infarction or haemorrhage relevant to the symptoms" (19). 'Minor' stroke is defined by a score of 3 or less on the National Institutes of Health stroke scale at initial assessment as per previous authors (20)(21).

2.2 Risk of stroke following a TIA - $ABCD^2$ score

The $ABCD^2$ score in TIA patients is used to identify the future risk of stroke (7) although the individual risk of subsequent stroke also varies with the underlying mechanism(s) involved (10)(17). The $ABCD^2$ score consists of:

Elements of ABCD^2 score	Points
Age 60 years or above	1
Blood pressure 140/90mmHg or above on first evaluation	1
Clinical symptoms of focal weakness with spell Or, speech impairment without weakness	2, OR 1
Duration of 60 minutes or more or 10-59 minutes	2, OR 1
And **D**iabetes	1

The points for each feature are added together to obtain the total ABCD^2 score for that TIA episode. The 90 day risk of stroke based on the ABCD^2 score is 3.1% when the score is low (0-3), 9.8% with a moderate score (4-5) and 17.8% with a high score of 6-7 (17).

2.3 Stroke Risk Factors

TIAs and strokes are most commonly caused by the embolic or thrombotic consequences of atherothrombotic disease (17), similar to the underlying pathological mechanism for cardiovascular disease (22) (23)(24). As well as sharing a similar underlying pathological mechanism, cerebrovascular and cardiovascular disease share common underlying risk factors (23)(25) and a high prevalence of asymptomatic coronary artery disease has been identified post-TIA (8)(24)(25)(26)(27).

The modifiable risk factors for all vascular diseases include smoking, excessive alcohol intake, physical inactivity, dietary factors, hypertension, dyslipidaemia, diabetes, and obesity (28) as well as low VO_{2max} (29)(30)(31)(32). Five modifiable risk factors are reported to account for 82% of strokes: hypertension, smoking, obesity, unhealthy diet and physical inactivity (33).

O'Donnell et al (34) conducted the INTER-STROKE study between 2007 and 2010, which was a population-based case-control study in 3,000 cases within twenty-two countries, to review stroke risk factors. Cases were those with a first stroke diagnosis and controls were those with no stroke diagnosis, matched for age and sex. Significant risk factors for all strokes (34) have been included in the below table and have been compared to risk factors for myocardial infarction from the INTER-HEART study (35) to illustrate the similarity in risks between cardio- and cerebro-vascular disease. The INTER-HEART (35) study is similar to INTER-STROKE (34)(36), being a case-control study but assessing the risk factors for coronary heart disease in 12,461 cases across 52 countries.

Risk factor	Risk for all strokes (Odds ratio, OR, 99% Confidence intervals, CI adjusted for age, sex and region)	Risk for myocardial infarction (Odds ratio, OR, 99% Confidence intervals, CI adjusted for age, sex and smoking)
History of hypertension	OR 2·64, 99% CI 2·26–3·08	OR 2.48, 99% CI 2.30-2.68
Current smoking	OR 2·09, 99% CI 1·75–2·51	OR 2.95, 99% CI 2.72-3.20
Waist-to-hip ratio (i.e. abdominal obesity, top 2 tertiles versus the bottom one)	OR 1·65, 99% CI 1·36–1·99	OR 1.36, 99% CI 1.24-1.48
Diet risk score (top 2 tertiles versus the bottom tertile)	OR 1·35, 99% CI 1·11–1·64	
Vegetable and fruits daily		OR 0.70, 99% CI 0.64-0.77
Regular physical activity/exercise	OR 0·69, 99% CI 0·53–0·90	OR 0.72, 99% CI 0.65-0.79
Diabetes mellitus	OR 1·36, 99% CI 1·10–1·68	OR 3.08, 99% CI 2.77-3.42
Alcohol intake (1-30 drinks/month)	OR 0.90, 99% CI 0.72-1.11	OR 0.79, 99% CI 0.73-0.86
Psychosocial stress	OR 1·30, 99% CI 1·06–1·60	OR 2.51, 99% CI 2.15-2.93
Depression	OR 1·35, 99% CI 1·10–1·66	
Cardiac causes	OR 2·38, 99% CI 1·77–3·20	
Ratio of apolipoproteins B to A1 (for stroke risk, the top 2 tertiles compared to the last whilst for myocardial infarction the 2nd quintile compared to the 1st)	OR 1·89, 99% CI 1·49–2·40	OR 1.47, 99% CI 1.28-1.68

Overall these risk factors account for approximately ninety per cent of the risk for stroke and this was confirmed on a more recent update of the INTERSTROKE study, published in 2016 (36). As can be seen from the table, these risk factors are very similar to that of myocardial infarction, that is, cardiovascular disease risk factors. Thus there are several lifestyle modifications that might contribute to a substantial reduction in the risk of vascular events post-TIA and there is evidence that the earlier these interventions can be introduced, the better the outcome (11)(37). National guidelines also state that TIA patients should be reviewed in a specific clinic within one week of the diagnosis (13), for the early introduction of prevention and rehabilitation.

Despite improvements in acute stroke care, prevention remains the cornerstone of reducing the stroke disease burden (38). Indeed a Cochrane review has highlighted the importance of tackling modifiable vascular risk factors for secondary prevention in those diagnosed with a TIA and/or stroke (16) but the review highlighted the need for further clinical studies in this area, with only one completed study included in the review.

2.4 Pharmacological Secondary Prevention of Stroke

National United Kingdom (UK) guidelines for the pharmacological treatment of stroke have been established by the National Institute for Health and Clinical Excellence (NICE) (13)(39) and the Royal College of Physicians (14) and are supplemented by guidelines on tackling individual risk factors. Following the acute diagnosis of stroke, anti-platelet medication is initiated unless contra-indicated. This typically takes the form of a prophylactic 75mg daily dose of aspirin although other agents, for example

dipyridamole and clopidogrel, may be added or used instead of aspirin. Statins are generally initiated to lower cholesterol levels (40) and appropriate anti-hypertensive medications utilised for blood pressure control as per national management guidelines (41).

2.5 Non-pharmacological/ lifestyle risk factor modification of stroke risk

2.5.1 Physical activity

The WHO (World Health Organisation) reports that:

> "Physical activity is a fundamental means of improving the physical and mental health of individuals." (42)

Physical activity promotion and participation must therefore be one of the key goals for modern-day health systems (43). Indeed good health is a key determinant of development and essential for economic growth (42). Moreover, the WHO in 2010 (44) identified physical inactivity as the fourth leading risk factor for global mortality and other authors (45) report that physical inactivity directly causes 5.4 million deaths per year, equivalent to the mortality risk of smoking and obesity combined.

Physical activity has been shown to reduce risk for cardiovascular disease, stroke and type II diabetes mellitus (43)(46)(47); it reduces blood pressure, improves the level of high density lipoprotein cholesterol, improves control of blood glucose in overweight people (47) and also reduces the risk for colon cancer and breast cancer among women (42)(48). High levels of moderate-intensity physical activity (60-75 minutes/day) also appear to eliminate the negative health and mortality effects of being sedentary (49). Moreover physical activity has positive effects on osteoporosis and the risk of falls

(50), on musculoskeletal conditions such as osteoarthritis (51) and low back pain and on mental and psychological health, by reducing depression, anxiety and stress (52)(53)(54).

Indeed Chan et al (46) undertook a cross-sectional study of sedentary workers' physical activity levels in Canada using a sealed pedometer and found a significant inverse correlation between steps/day and BMI, female waist circumference and diastolic blood pressure. Inactivity was also found to be associated with ischaemic heart disease, hypertension, hypercholesterolemia and diabetes (46).

Exercise is essential in the management of type II diabetes mellitus, which patients with a TIA and/or stroke may have. Tudor-Locke et al (55) conducted a randomised controlled trial of a pedometer-based exercise programme over 16 weeks in 60 people from Ontario diagnosed with type II diabetes mellitus and treated with diet and/or oral hypoglycaemic agents. The authors found an increase of 3,000 steps/day from baseline associated with a 1.8cm reduction in waist girth at the end of the 16 weeks. Steps/day at baseline was also found to be inversely correlated with blood glucose, HbA1c and triglyceride concentrations in those treated with oral hypoglycaemic agents. Thus, being more active helps improve plasma glucose control in type II diabetes mellitus and helps reduce the cardiovascular risk associated with this chronic condition.

With regards the antidepressant effect of exercise, Rethorst's review article (54) highlights that exercise has an equivalent antidepressant effect to antidepressant medication and a better antidepressant effect than psychotherapy, which is important as depression is a recognised risk factor for vascular disease (56). That is, physical activity:

> "has the capacity not only to add years to life, but to bring life to years". (57)

Despite the benefits of physical activity being clear, 54% of men and 60% of females in Northern Ireland (NI) do not meet the current physical activity guidelines as per the NI Sport and Physical Activity Survey (SAPAS) report (58)(59). The NI SAPAS report was conducted via in-home interviews using a stratified random sample of NI households, to allow an assessment of the physical activity levels of the population. Physical inactivity is a clear risk factor for further vascular events and needs to be clearly promoted to patients who have recently suffered a TIA and/or 'minor' stroke (43).

2.5.2 Cardiorespiratory fitness

Cardiorespiratory fitness, measured by VO_{2max}, is inversely correlated with mortality (29)(30)(31)(32), with the progression of carotid atherosclerosis (60) and with the risk of stroke. Myers et al (61) found that in male subjects with and without cardiovascular disease, peak exercise capacity after adjustment for age, was the strongest predictor of the risk of death and each one metabolic equivalent (MET) increase in exercise capacity conferred a 12% improvement in survival. Meanwhile Kurl et al (62) in a population-based cohort study in Eastern Finland of 2011 men with no history of stroke or coronary heart disease, with an average follow-up of twelve years, found that an increase in VO_{2max} of 3.5 ml/kg/min was associated with a 17% decrease in stroke risk. This finding has been confirmed in a meta-analysis (63). Meanwhile previous authors have shown that cardiorespiratory fitness is reduced at one month (64) and up to 12 months (65) post-stroke compared to age- and sex-matched controls.

Exercise can increase VO_{2max} in sedentary persons (66) and in sub-acute stroke survivors (67). Indeed Duncan et al (67) conducted a pilot study of an assessment of

the impact of an eight week home-based therapist-supervised exercise programme undertaken three times a week in patients who had suffered a mild to moderate stroke thirty to ninety days previously and showed an improvement in the six minute walking test performance in the intervention group. However their study did not include patients in the acute phase following the initial stroke diagnosis. There is a paucity of published data linking post stroke/TIA exercise to change in subsequent stroke risk.

2.5.3 Smoking

Smoking is a well-recognised vascular risk factor. The landmark prospective observational study by Doll et al (68) found that British male doctors born between 1900 and 1930 who continued to smoke, had a life expectancy that was ten years less than that of life-long non-smokers. Smoking has been identified as a vascular risk factor in many other studies (15)(34)(69), with those who currently smoke having a 2 to 4 times higher risk of having a stroke compared to life-long non-smokers or to those who have stopped smoking more than 10 years previously (70).

2.5.4 Diet

With regards diet, the 'Mediterranean diet' has shown favourable effects on cardiovascular risk factors (71) and reduced salt intake improves blood pressure control, reducing the risk of cerebrovascular events (72). A recent meta-analysis has also shown that dietary fibre is inversely correlated with the risk of stroke (73) and being overweight increases your overall mortality risk (74). Thus weight loss is an important health message to advocate to patients. Moreover hypercholesterolaemia, of which dietary intake may be a source, is a modifiable risk factor for cardio- and

cerebro-vascular disease (75) and cholesterol levels were found to be positively associated with the risk of nonhaemorrhagic stroke (76). Dyslipidaemia was also identified as a significant risk factor for ischaemic stroke in the INTERSTROKE study (77), which was a case-control study across 22 countries.

2.5.5 Stress

Psychological distress is a known risk factor for TIAs and strokes. Indeed in the observational study by Everson-Rose et al (78), 6749 adults free of cardiovascular disease at base-line in the United States, aged 45 – 84 years old, were followed up for a median of 8.5 years as part of the Multi-Ethnic Study of Atherosclerosis (MESA). The authors found that higher levels of stress and depressive symptoms were associated with increased stroke and TIA risk, independent of other known vascular risk factors. Moreover the diagnosis of TIA and/or stroke often leaves survivors with stress, anxiety and depressive symptoms, with a recent systematic review (79), highlighting the prevalence of these often forgotten symptoms following a TIA and/or stroke diagnosis.

2.5.6 Alcohol

Alcohol excess is a well-known modifiable vascular risk factor, including for TIAs and strokes. Gill et al (80), report the 'J-shaped' association between alcohol and risk of stroke in a case-control study of approximately 1,200 patients. That is, alcohol at low levels may have a protective effect for cerebrovascular events, whereas heavy consumption predisposes to stroke. This is supported by a recent Swedish cohort study (81), following up 811,579 Swedish men from a mean age of 18, which found that

alcohol excess was an independent modifiable risk factor for stroke. Restriction of alcohol consumption should therefore be promoted to the population to reduce the risk of future TIA and stroke events (82).

3.0 - Secondary prevention of stroke

3.1 The 'evidence gap' from research to practice

Despite the knowledge surrounding vascular risk factors and the recognition that TIA and 'minor' strokes are often the precursors of disabling strokes, more needs to be done in reducing stroke as the leading cause of adult disability (83). Indeed the World Health Organisation (WHO), as part of their 2013 Global Action Plan For the Prevention and Control of Non-Communicable Diseases, has targeted a 25% relative risk reduction in premature mortality from cardiovascular diseases, including TIAs and stroke (84).

3.2 Physical activity and pedometer use in stroke

Physical activity is an important component of the strategy to meet the WHO 2013 Global Action Plan targets (84). One method of promoting physical activity and potentially improving VO_{2max}, two known vascular risk factors, is through the use of pedometers (85). Pedometers are commonly used to provide a measurement of physical activity, to provide patient feedback and as a motivational instrument through goal setting. Pedometers can be used with different Behaviour Change Theories, for example, the theory of planned behaviour (86).

Pedometers have been shown to be accurate and reliable in measuring ambulatory activity (46)(87)(88)(89) whilst also being relatively inexpensive. Yamax pedometers have been shown to be the most accurate waist-borne instrument (87) and total daily step count is an accurate descriptor of ambulatory activity (87)(88). Pedometers appear feasible for use by patients with stroke although their accuracy at slow walking speeds

has been questioned (90)(91). No reports have been identified regarding the use of pedometers as a physical activity promotion tool by patients with TIA or within the acute stroke setting and indeed a recent systematic review on the role of cardiovascular exercise post-stroke, has highlighted the lack of studies of this tool in the acute and sub-acute periods (92).

Pedometer step counts correlate with cardiovascular health (88) and higher daily step counts are linearly associated with subsequent lower mortality (93). Increasing steps/day by an average of 2,500 led to modest weight losses and a mean reduction in systolic blood pressure of 3.8mmHg (94). Significant decreases in BMI and blood pressure have also been associated with a similar step count increase of 3,000 steps/day (88)(95).

Moreover, physical activity public health recommendations have been translated into pedometer targets (94). A cadence of approximately 100 steps per minute is considered the floor value for moderate-intensity activity (88) and approximately 130 steps per minute is congruent with vigorous intensity activity although it has been suggested that stride rates for specific walking intensities should be adjusted for an individual's height (96). Step-counts can therefore be used by patients to achieve the recommended levels of physical activity, including both the amount and intensity, helping to tackle the known vascular risk factor of physical inactivity. Pedometers also appear to promote physical activity in the long-term, with De Cocker et al (97) showing that after 4 years of follow-up, the pedometer intervention group had higher physical activity levels than the control group.

3.3 Risks of physical activity in stroke

Exercise guidelines for stroke survivors have been established (98), with exercise in this cohort of patients considered to be safe (98) and to produce recognised health benefits (99)(100). A twelve week supervised exercise programme in sub-acute stroke survivors demonstrated improvements in flexibility, strength, endurance, mobility and balance, with no excessive adverse events reported (101).

A supervised cardiac rehabilitation programme is reported to be safe in stroke survivors (102)(103)(104) and community-based exercise programmes are safe and effective in those who have had a stroke (105)(106). Moreover, the risk of any major cardiac event during cardiac rehabilitation, performed in a similar patient cohort to TIA and stroke patients, has been estimated as one event in 60,000 to 80,000 hours of supervised exercise (107).

4.0 Stroke and cardiovascular disease: pathological mechanisms and rehabilitation

4.1 Cardiac rehabilitation and myocardial infarction

Although cardio-vascular and cerebro-vascular disease share common underlying pathological mechanisms and risk factors, cardiac rehabilitation for secondary prevention is only offered to patients in the UK with cardiovascular disease (108), despite current scientific statements promoting its use in secondary prevention following a stroke (109). The WHO has defined cardiac rehabilitation as the:

> "sum of activity and interventions required to ensure the best possible physical, mental and social conditions so that patients with chronic or post-acute cardiovascular disease may, by their own efforts, preserve or resume their proper place in society and lead an active life" (110).

NICE have recommended that the components of cardiac rehabilitation should include exercise, health education and stress management (108), helping to tackle the known vascular risk factors as previously documented in this Chapter. Health education would include addressing the known modifiable vascular risk factors as well as providing advice regarding work, mental health and sexual activity (108). These components are all addressed in the "Heart Manual" (111), a home-based cardiac rehabilitation programme.

The "Heart Manual" is the only validated home-based cardiac rehabilitation programme supported by NICE for patients who have had a myocardial infarction (MI) (112). It is based on the Health Belief Model of behaviour change theory and uses cognitive behavioural techniques, including goal setting, and its use has been associated with reductions in depression, anxiety and cholesterol levels and improved

quality of life (113). The “Heart Manual” has also been associated with reductions in blood pressure, improved exercise capacity and smoking cessation rates that are comparable to those achieved with hospital-based cardiac rehabilitation programmes (114). Other work has also shown that use of the “Heart Manual” has been associated with reduced anxiety and depression, strengthened illness control beliefs (115) and increased confidence in recovery and self-perceived progress (116).

Cardiac rehabilitation after a MI results in a statistically significant reduction in re-infarction (odds ratio 0.53, 95% CI 0.38 – 0.76), cardiac mortality (odds ratio 0.64, 95% CI 0.46 – 0.88), and all-cause mortality (odds ratio 0.74, 95% CI 0.58 – 0.95) (117). These findings concur with those of a Cochrane Review (118) although it was acknowledged that the studies included in the review mainly included middle-aged men who are generally at low cardiovascular risk. A recent review by Rauch et al (119) illustrated the continued benefit of cardiac rehabilitation despite recent advances in medical and surgical treatments.

A Cochrane Review demonstrated hospital- and home-based cardiac rehabilitation programmes, most of which used the “Heart Manual”, could result in similar health gains (120), with home-based programmes improving adherence to the programme (121). This finding was again found in a recent Cochrane systematic review (122), illustrating that home-based cardiac rehabilitation produces similar health benefits to centre-based options. Moreover, home-based cardiac programmes have shown longer term sustainability of health benefits compared with hospital-based programmes (123).

Thus there is strong evidence via meta-analysis and systematic reviews to support the use of a home-based programme in a patient population with cardiovascular disease. Furthermore, it may be hypothesised that it would also have value in the secondary

prevention of cerebrovascular disease, which shares underlying pathological mechanisms and risk factors with cardiovascular disease.

4.2 Cardiac rehabilitation and stroke

Lennon et al (124) and McKay-Lyons et al (28) have described randomised trials of community-based cardiac rehabilitation programmes in both TIA and stroke patients. These studies did not review the use of home-based programmes, which we know are at least as effective as community-based options whilst being more cost-effective (122), and did not include a pedometer arm. These studies finished early, with no results available in their clinical trials registry entries or published. Both described a relatively long period from the event to entry into the trial (up to 90 days for both studies). However other research has shown that vascular risk factors should be addressed as quickly as possible following the initial vascular event (11).

Prior et al (103) have described a pilot study of a community-based cardiac rehabilitation post-TIA and 'mild' stroke and showed important reductions in biological markers linked to cardiovascular and cerebrovascular mortality. Approximately half of the TIA/"minor" stroke patients who were approached to enter the study consented to participate and roughly 80% of people who consented to participate in the study completed the study. Thus community cardiac rehabilitation programmes appear feasible in this patient group. Moreover Prior et al (103) report that they achieved significant changes in aerobic capacity, lipid profile, waist circumference, body mass index, body weight and smoking status at six months compared to baseline. There was also a statistically non-significant reduction in BP and HDL cholesterol. However the study did not include a control group, patients were eligible for inclusion up to one year post-event and the researchers did not offer home-

based rehabilitation and did not include pedometers in the rehabilitation programme. Other authors have also piloted community-based cardiac rehabilitation programmes in the TIA and minor stroke population, with patients eligible for inclusion up to one year post-event (125)(126) but no authors have previously assessed the feasibility of adapting a home-based cardiac rehabilitation programme, with or without an added pedometer intervention, initiated within the first month post-event for this patient population.

Therefore the use of cardiac rehabilitation programmes post-TIA/'minor' stroke requires further research. Such research has immediate clinical significance and the potential to change guidelines for the management of TIAs and minor strokes, as well as the potential to reduce morbidity and mortality resulting from TIAs and strokes in Ireland and the UK, with clear benefit to patients.

5.0 Conclusion

5.1 The research question

The literature shows the importance of stroke prevention and its relevance to healthcare services. The evidence presented in the earlier sections of this Chapter shows the significance of implementing early prevention after a TIA or minor stroke and this has been supported by a recent editorial in the Lancet (4). There are gaps in the evidence regarding the translation of secondary prevention initiatives from research into practice and a lack of evidence regarding the best approach to promoting secondary cardiovascular prevention to reduce subsequent stroke risk for patients with a TIA or minor stroke. However, cardiac rehabilitation, which combines approaches to lifestyle change with the provision of appropriate medication, is effective for reducing risk for patients with cardiovascular disease and there is a suggestion that a similar approach to patients with TIA or minor stroke may be effective. The research question that this thesis seeks to explore was:

- Can a novel home-based rehabilitation programme, '*The Healthy Brain Rehabilitation Manual*', with the use of an additional pedometer, be developed for use in patients with a first TIA or 'minor stroke of atherosclerotic origin, utilising the core components of home-based CR.
- I then wanted to test the practicality of using the intervention within feasibility and pilot studies and receive appropriate qualitative review of the intervention at each stage of its development.

5.2 Research objectives

The overall aim of this project was to develop a novel home-based rehabilitation programme, '*The Healthy Brain Rehabilitation Manual*', for patients with transient ischaemic attack (TIA) and/or 'minor' stroke and to determine the feasibility of conducting a randomised controlled trial to evaluate its effectiveness. The project aimed to use the Medical Research Council (MRC) guidelines for developing complex health service interventions (127) and the home-based cardiac rehabilitation manual, the "Heart Manual" (111), in the development of the novel programme.

It was hypothesised that the "Heart Manual" would be able to be adapted to develop a rehabilitation programme ('*The Healthy Brain Rehabilitation Manual*') for patients with a TIA/'minor' stroke. It was also hypothesised that the programme would be perceived as being acceptable, relevant and valuable to patients, and that feasibility and pilot studies would show that its effectiveness could be tested in a randomised controlled trial, with potential for real-world patient benefit. The studies included an added pedometer intervention and tested if a specialist stroke nurse or a General Practitioner (GP) could deliver these interventions effectively.

The proposed trial was the first to assess the effect of a home-based vascular rehabilitation programme on secondary cardiovascular risk factors in patients early after their first 'minor' stroke or TIA. The study was also the first to assess the acceptability of such an approach and the use of pedometers to increase physical activity levels in the acute TIA and 'minor' stroke setting. Pedometers act as a tool to prompt physical activity and provide a means of objective personal feedback regarding achievement of goals and promote longer-term behaviour change. The study also

attempted to assess how best to deliver the intervention through utilising either a stroke nurse or a GP. The intervention proposed for this trial was based on an effective home-based cardiac rehabilitation programme, the ‘Heart Manual’, and incorporated characteristics shown to maximise adherence whilst emphasising early intervention, being initiated within four weeks of the TIA or ‘minor’ stroke to maximise patient benefits.

Chapter 2

Rehabilitation Programmes with Secondary Prevention Lifestyle Interventions Initiated within 90 days following a TIA or 'minor' stroke: Systematic Review and Meta-analysis

Aims

This section of the thesis was a systematic review of comprehensive rehabilitation programmes that included secondary prevention lifestyle measures, initiated within 90 days of a TIA and/or 'minor' stroke. It aimed to examine the effects of these programmes and to identify the 'active' ingredients in each by identifying the behaviour change techniques (BCTs) that had been utilised. The information from this systematic review of the literature was then used in the initial development of '*The Healthy Brain Rehabilitation Manual*'.

Objectives

This review aimed to investigate the effect of comprehensive rehabilitation programmes that included secondary prevention lifestyle measures, initiated within 90 days of a TIA or 'minor' stroke in adults and to identify and categorise the BCTs (128) that were employed in these programmes.

Introduction

There is a need for clearer guidance regarding optimal early prevention and rehabilitation strategies and interventions to promote lifestyle change following TIAs and 'minor' strokes. Some current guidelines (129)(130) advocate the promotion of early non-pharmacological secondary prevention after all cerebrovascular events but lack detail regarding effective methods of their delivery. There have been reports of lifestyle interventions post-TIA and minor stroke (131)(132)(133). However, no previous systematic reviews of the evidence of the effectiveness of early post-TIA

rehabilitation or secondary prevention programmes that describe non-pharmacological and lifestyle interventions have been identified.

Whilst TIA and 'minor' stroke patients are typically without residual physical functional disability, they often have residual functional impairment, particularly with regard to post-event fatigue and psychological issues which may lead to more significant disability (79)(134). These issues, however, are not highlighted currently within early rehabilitation or secondary prevention programmes for patients with TIA/minor stroke, although the novel adaptation of cardiac rehabilitation programmes for TIA and stroke patients has been advocated (103)(124)(125).

Comprehensive programmes, which try to alter participants' behaviours, are complex: information about their 'active' ingredients, such as specific BCTs (128), would facilitate their replication and the implementation of guidelines for good clinical practice (135)(136). Thus this systematic review was undertaken to help produce an evidence base upon which rehabilitation interventions can be developed for this patient group, particularly within the acute period following the diagnosis of a TIA or 'minor' stroke.

Methods

This systematic review is reported in line with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidance (137) and has been reported as per previous authors (138). The study protocol was published prior to starting the review (139). I planned to include human randomised and quasi-

randomised controlled trials of rehabilitation programmes initiated within 90 days of patients suffering a TIA or minor stroke.

The review focused on adults, males and females, aged 18 years or older, that received a diagnosis of a TIA and/or 'minor' stroke, based on clinical diagnosis, or on findings from brain imaging (e.g. CT or MRI head). Studies that included only moderate or severe stroke patients, which did not provide outcome data specifically for patients with TIA/minor stroke and/or in which the intervention was initiated later than 90 days post-event were excluded.

Any rehabilitation programme, identified as a set of measures to achieve and maintain a patient's optimal functioning (83), following an initial TIA or 'minor' stroke, was eligible for inclusion. The review included any 1:1 or group-based intervention which was undertaken in hospital, outpatients, community or the home, trials with a comparative control group and trials with multiple intervention arms (comparing different forms of rehabilitation). The review did not include population or community-wide interventions.

Types of outcome measures

i) Primary outcomes

• Quantitative between-group differences for modifiable cardiovascular risk factors (e.g. blood pressure, lipid and triglyceride profiles, markers of insulin resistance and obesity, validated cardiovascular risk score, measures of physical activity, tobacco use) or level of functioning and/or disability, including social and emotional functioning.

ii) Secondary outcomes

- Secondary cardiovascular events: stroke, myocardial infarction, or vascular death.
- Any adverse events (e.g. exercise-related musculoskeletal injuries).
- Any indicator of patient adherence to secondary prevention medication, e.g. self-reported medication adherence.

Search methods for identification of studies

Detailed search strategies were developed for each electronic database searched with input from a medical librarian to allow identification of studies for inclusion in this review. The searches were based on the strategy developed for Medical Literature Analysis and Retrieval System Online (MEDLINE) (**Appendix 1**) but revised appropriately for each database. I searched the Cochrane Library, Ovid MEDLINE(R) 1946 to March 2015, Ovid Embase 1974 to March 2015, Web of Science, EBSCO Cumulative Index to Nursing and Allied Health Literature (CINAHL) plus 1937 to March 2015 and Ovid PsycINFO 1806 to March 2015. Any systematic reviews of rehabilitation interventions in the acute period following a TIA or 'minor' stroke were screened for additional references. The titles and abstracts of publications from the search strategy were independently screened by myself and a supervisor (NH 100%, MEC 100%). Additional studies were identified from reviewing the reference lists of the retrieved papers through a hand search. Articles not meeting the inclusion criteria were discarded. A standardised form (**Appendix II**) was used to select the trials eligible for inclusion in the review with, if necessary, a second supervisor (FK) resolving disagreements. A record was kept of all articles excluded at this stage and

the reason for their exclusion. No language restrictions were made although all papers were written in the English language.

Data on methodological issues, eligibility criteria, interventions (including the number of participants treated, intervention provider) and study design, study duration, follow-up, comparisons, outcome measures, results, withdrawals and adverse events were extracted independently by myself and a supervisor (NH, MEC). There was no blinding to study author, institution or journal and a record was kept of each study included in the review.

Assessment of quality and risk of bias

The PEDrO scale (140) was used to assess the quality of included papers in the review. Also, I and one supervisor (MEC) independently assessed each included study for risk of bias ('high', 'low' or 'uncertain') using the risk of bias tool, following guidance from the Cochrane Handbook of Systematic Reviews of Interventions (141), a second supervisor (FK) acting as arbitrator as required.

Measures of treatment effect

For each study, relative risk and 95% confidence intervals were calculated for dichotomous outcomes and mean differences and 95% confidence intervals were calculated for continuous outcomes. Where continuous outcomes were pooled on different scales, standardised mean differences were used. Where available, changes from baseline (mean change scores) were used in preference to follow-up scores. When combining results for the individual studies, I generally used mean differences

and a random effects model apart from two variables, deaths and falls, when I used odd ratios with a random effects model.

Assessing for heterogeneity

Diversity across the studies was assessed qualitatively in terms of intervention (content, duration, frequency, provider and setting), participant demographics, outcome measures and follow-up. If two or more studies were considered clinically homogenous according to the above terms, data were assessed for statistical heterogeneity using RevMan version 5.1. The chi-squared ($\chi 2$) test was used in conjunction with the I^2 statistic, which describes the percentage of variability in effect estimates due to heterogeneity. The level of significance for the $\chi 2$ was set at $p < 0.1$. Values of I^2 from 30% to 60% were considered to represent moderate heterogeneity and 60% to 90% substantial heterogeneity (141).

Data synthesis

Careful consideration was given to the appropriateness of conducting a meta-analysis. Data were summarised statistically when the data were available, sufficiently similar and of sufficient quality and the statistical analysis was performed in accordance with guidelines (141).

Behaviour change techniques (BCTs)

Two trained review authors (NH, MAT) independently screened studies included in the review for the reported use of BCTs. Michie's BCT taxonomy (128), comprising 93 hierarchically clustered techniques, was used to identify the BCTs and a narrative approach was used to describe their use within the rehabilitation programmes.

Results

I reviewed the full text of 47 studies and identified 31 studies for possible inclusion in this review (**Figure 1**). Only two of the 31 studies were included and an additional two studies were retrieved from the reference lists of the previously identified 31 studies (see **Table 1)**; 3 papers could not be traced. Fourteen studies were excluded because the sample comprised participants with moderate or severe stroke and six studies were excluded because they included participants with varied stroke severity and did not provide outcome data for patients with TIA/minor stroke. A further 6 studies were excluded because they were protocols (2), editorials/overviews (2) or did not have appropriate outcome measures (2).

Programme design and evaluation

Four studies were included in the review. Allen et al, 2009 (142) evaluated whether a comprehensive post-discharge care management for 380 minor stroke survivors was superior to organised acute stroke department care with enhanced discharge planning. Toledano-Zarhi et al, 2011 (143) examined the feasibility, safety and effectiveness of an early aerobic rehabilitation programme for 28 patients between one and three weeks

post minor ischaemic stroke. Boysen et al, 2009 (144) investigated the effect of repeated verbal instructions about physical activity delivered to 314 patients within 90 days of a minor ischaemic stroke, three-monthly for the first year and six-monthly for a second year. Tanne et al, 2008 (145) assessed the tolerability, safety and effect of an outpatient supervised exercise training programme, in 52 patients after a non-disabling stroke, initiated within a mean time of 65 days. Two of the included studies were conducted in Israel (143)(145), one in the United States (142) and one in China and Europe (Denmark, Poland, and Estonia) (144). All patients had a diagnosis of TIA and/or 'minor' ischaemic stroke and were recruited from secondary care, typically from stroke units. Three studies delivered the intervention in secondary care (143)(144)(145) whilst one (142) was delivered at home by a multi-disciplinary team after an initial consultation in hospital. Outcomes were assessed after 6 weeks (143), 3 months (145), 6 months (142) and 2 years (144).

Behavioural Change Techniques in Included Studies

The BCT identified as, 'instruction on how to perform a behaviour', was employed in all four studies. 'Goal setting' was used in three of the four studies and a range of other BCTs was used by different studies (**Table 2**). One outpatient exercise programme (145), a feasibility study, was the only programme that used the BCT of 'discussing behavioural consequences' with patients and this study reported a statistically significant improvement in post-event exercise capacity.

Within the BCT Taxonomy (128), individual BCTs are clustered into hierarchical groups that commonly appear together in behavioural interventions. The commonest group of BCTs used in the 4 included studies was 'goals and planning', whilst the

second most common group utilised was ‘sharing knowledge’. Of all the groups of BCTs listed in the taxonomy (128), 5 did not appear within any of the studies: these were ‘reward and threat’, ‘antecedent identity’, ‘scheduled consequences’, ‘self belief’ and ‘covert learning’.

Regarding use of the BCT ‘instruction on how to perform a behaviour’, one study reported that a physiotherapist or neurologist provided “repeated encouragement and verbal instructions on being physically active” (144). Toledano-Zarhi et al (143) reported that they provided all participants with a home exercise booklet, including information on strength and flexibility exercises, as well as encouraging them to maintain their normal physical activity routine in the community. The participants in the active group then additionally received a supervised exercise programme twice weekly for 3 hours per week over a duration of 6 weeks. Meanwhile in Tanne et al (145) the intervention group were entered into a supervised exercise training programme performed twice weekly over a 3 month duration. A physiologist prescribed the exercise programme, with specific guidance regarding intensity, type and duration of exercise. Allen et al (142) reported that they offered general lifestyle modification advice to address secondary prevention factors.

Risk of bias in included studies

Allen et al, 2009 (142) and Boysen et al, 2009 (144) were deemed to be at low risk of bias whilst Tanne et al, 2008 (145) was assessed as being at high risk of bias as it was a pilot, quasi-randomised controlled trial **(see Table 1)**. Toledano-Zahri et al, 2011 (143) was assessed as being at uncertain risk of bias as there was no detail reported regarding randomisation or blinding of participants and assessors. The application of

the PEDrO scale (140) supported these assessments. Allen et al, 2009 (142) and Boysen et al, 2009 (144) had allocation concealment within their study design, thus reducing their risk of bias, in contrast to Tanne et al, 2008 (145) and Toledano-Zarhi et al, 2011 (143). The paper by Allen et al, 2009 (142) is unclear regarding blinding of participants and personnel for study allocation but outcome measurements were blinded. Tanne et al, 2008 (145) and Toledano-Zarhi et al, 2011 (143) did not detail how their groups were allocated or if personnel were blinded to study allocation. Boysen et al, 2009 (144) described how personnel undertaking their outcome assessment, the Physical Activity Scale for the Elderly (PASE), were blinded to group allocation. The proportion of study participants completing follow-up ranged from 92% in the intervention arm (144) to 100% (142)(143). All studies fully accounted for the study participants and provided reasons for any missing data. No other potential sources of bias were identified.

Assessment of reporting bias

Funnel plots were not produced as only two studies were included in each of the outcome measures.

Outcomes

One study reported the percentage dead at the end of study, percentage smoking and percentage exercising (142); one reported change in the PASE, number of vascular events and change in modified Rankin Scale (144) and two (143)(145) shared similar outcome measures (six minute walk test (6 MWT), exercise test results (metabolic

equivalents (METS) achieved) and resting and peak blood pressure). Although there was a high risk of bias in Tanne's work (145) and an uncertain risk of bias in the study by Toledano-Zahri (143), their results were included in a meta-analysis, to explore potential insights, whilst being cautious about interpretation. A sensitivity analysis was not undertaken because the results of the meta-analysis were non-significant.

The overall treatment effect showed no improvement in the resting systolic blood pressure (**Figure 2)** or in peak systolic blood pressure. There was no treatment effect for resting heart rate nor for the 6MWT (**Figure 3**), although improvement in the 6MWT was shown by one study, a three month outpatient exercise programme (145). The overall treatment effect showed no improvement in the exercise testing result (**Figure 4**), although one study showed improvement in metabolic equivalents (METs) (145). There was no effect shown on the number of falls experienced by the participants during the rehabilitation programme or in rates of death following the rehabilitation programme. Of note, two studies (143)(145) reported no deaths during their studies and so these results were unable to be incorporated into the meta-analysis.

Discussion

This systematic review comprised four studies that initiated rehabilitation programmes that included lifestyle and non-pharmacological interventions within 90 days of a diagnosis of TIA or 'minor' stroke, though only two studies were of high methodological quality. Many other potentially eligible studies were excluded from the review because they did not present results specifically for patients with TIA or minor stroke. This highlights that previous secondary prevention rehabilitation programmes have focused on moderate and severe stroke patients. A meta-analysis

found no evidence of significant effects on subsequent stroke risk or on vascular risk factors although two studies reported improved measures of exercise capacity (143)(145).

This review, the first to report collated observations on the BCTs used in studies of rehabilitation programmes for patients with acute TIA or minor stroke, suggests that providing individualised instruction to patients about how to perform specific behaviours and behavioural goal setting, are key programme components but many other BCTs have been used. One programme, which reported improved exercise capacity (145), was the only one that included discussion of behavioural consequences with patients, hinting at the importance of using this BCT in future programmes. As the emphasis on early recognition of stroke and TIA in clinical practice increases, it is important to know more about appropriate comprehensive management programmes for these patients who may not have obvious residual disability and whose need for non-pharmacological support and rehabilitation may be overlooked.

Comparison with previous literature

Evidence is growing regarding the contribution of change in modifiable risk factors to reductions in cardiovascular deaths (15) and there is a need to consider how to promote non-pharmacological measures within secondary prevention (16). Indeed five modifiable risk factors are reported to account for 82% of strokes: hypertension, smoking, obesity, unhealthy diet and physical inactivity (33). A pilot study of a community-based cardiac rehabilitation post-TIA and ‘mild’ stroke, for patients up to one year post-event, showed reductions in biological markers linked to cardiovascular and cerebrovascular mortality, including aerobic capacity, lipid profile, waist

circumference, body mass index, body weight and smoking status at six months but did not include a control group (103). Similarly, Kirk et al (125) found that community-based cardiac rehabilitation programmes for 12 post-TIA and minor stroke patients can be effective at reducing modifiable vascular risk factors. Reviews identifying effective components of rehabilitation following the diagnosis of a TIA and 'minor' stroke have begun to emerge (131)(132)(133)(146) but, to our knowledge, this is the first systematic review of the use of rehabilitation programmes in the acute period (within 90 days) of the diagnosis of a TIA or 'minor' stroke.

No significant effect on vascular risk factors was found within this review, which is a similar finding to a recent systematic review assessing lifestyle interventions after TIAs and stroke (147), which only found an improvement in systolic blood pressure in their analysis. However, Brook et al (148) reviewed non-pharmacological treatment effects on blood pressure and found Class 1, level A evidence for the blood pressure lowering effects of exercise in patients with cardiovascular disease. Billinger et al (149) performed an eight week exercise programme in ten moderate severity stroke subjects in the sub-acute period following their diagnosis, with a reduction in resting heart rate and improvement in six minute walking test (6MWT) performance post-intervention. Duncan et al (150) found that an eight week home-based therapist-supervised exercise programme undertaken three times a week within 30 to 90 days of a mild to moderate stroke improved 6MWT performance in the intervention group. These 2 studies are supported by a recent meta-analysis (151), which found that exercise interventions in those with chronic disease, including stroke patients, can improve functional capacity and reduce disability in these patients, improving their quality of life. However, MacKay-Lyons et al (152) showed no change in peak systolic blood pressure when following stroke survivors, undifferentiated by severity,

for six months despite improvements in aerobic capacity. Thus, whilst previous work shows improvements in vascular risk factors associated with exercise for stroke survivors, our review highlights the lack of evidence of this effect following rehabilitation programmes initiated early after a TIA and/or 'minor' stroke. This is clearly an important area that requires urgent further research.

No significant reduction in the number of falls was found. However, Taylor-Piliae et al (153) found that exercise, particularly Tai Chi based programmes, improved balance and reduced falls in patients aged over 50 years, who had suffered a stroke up to three years previously. A recent systematic review and meta-analysis including 88 trials and 19,478 participants (154), showed that exercise can prevent falls in community-based older people, with programmes of a higher dose producing larger effects, stating that programmes which consist of a high challenge to balance and last for more than 3 hours/week have the greatest fall prevention effects, reducing fall rates by 39%. However a Cochrane review (155) has shown no consistent evidence for exercise programmes preventing falls in stroke survivors. Thus the evidence is mixed in relation to the effects of exercise on falls reduction post-stroke and further high-quality studies are required in this area.

No excess deaths were found in those undergoing rehabilitation programmes compared to those not undergoing rehabilitation and thus acute and sub-acute rehabilitation programmes appear safe in this patient cohort. Indeed exercise guidelines for stroke survivors have been established (98), with exercise in this cohort of patients considered to be safe (98).

NICE published guidance in 2014 on individual-level behaviour change interventions for promoting change in modifiable cardiovascular risk factors (136). These

guidelines recommended that behaviour change programmes, including lifestyle management programmes, should include BCTs relating to goals and planning, feedback and monitoring, and social support. In keeping with these guidelines (136), the most frequent BCTs found within this review were facilitating patients to set goals for behavioural changes and providing instruction on how to perform the new behaviours. However, the provision of social support was only implemented in two of the four studies (142)(144). These specific BCTs represent only a small fraction of those available in Michie's taxonomy, so that there is clear scope for further research. Moreover, this review highlights the poor reporting of BCTs used within interventions. It is clearly important to identify the specific BCTs used within studies to allow their replication. Future studies of rehabilitation and secondary prevention following a TIA and 'minor' stroke should therefore develop descriptions of the use of these techniques within their interventions.

Strengths and Limitations

A limitation of the review was the lack of consistency in the outcome measures used in included studies and combining results in a meta-analysis was therefore difficult. Another study limitation related to the duration of follow-up, which varied from six weeks to two years. The results should therefore be interpreted with caution, as shorter study durations may not allow sufficient time for the rehabilitation interventions to produce an impact on modifiable vascular risk factors.

Intervention intensity is generally a poorly defined concept (146), and differences in this are considered to be a source of heterogeneity within complex interventions (146).

Intervention intensity was different across the included studies and could be a potential source of bias within the review.

A comprehensive search strategy attempted to identify all studies of potential relevance to this review and this was supported through hand searching reference lists of all the full text articles examined. All eligible studies regardless of publication language were sought, although all studies were in English. Visual inspection of funnel plots did not raise any concerns regarding publication bias although this was limited as generally only two studies were included for each outcome measure.

This systematic review and meta-analysis is limited by the few studies available in this expanding and novel area of research; only four met the inclusion criteria. The search strategy focused on 'rehabilitation' rather than secondary prevention programmes, so that it is possible that potentially relevant studies may have been missed. However, this has served to highlight the lack of research focus on rehabilitation or early initiation of lifestyle interventions in secondary prevention for patients with TIA. The most common reasons for exclusion of potentially eligible studies were that they included moderate and severe strokes, with no focus on TIA and minor stroke or outcomes not specified for these patients. Another common reason to exclude potentially eligible studies was that the rehabilitation programme was not initiated in the acute period following diagnosis.

Conclusions

Few studies have reported the effects of early initiation of rehabilitation programmes, with or without pharmacological interventions, on secondary prevention for patients

with a TIA or ‘minor’ stroke. Rather, the focus of previous work has been on patients with ‘moderate’ and ‘severe’ strokes. This review has identified gaps in knowledge regarding the effectiveness of rehabilitation programmes, that include non-pharmacological and lifestyle measures, initiated in the acute period following a TIA or ‘minor’ stroke when the risk of further vascular events is highest. Further randomised controlled trials that include lifestyle interventions and details regarding the behaviour change techniques utilised for these patients are needed.

Chapter 3

Behaviour change techniques in home-based cardiac rehabilitation programmes for patients with cardiovascular disease: a systematic review

Aim

This section of the thesis was another systematic review but this time I wanted to identify and describe the use of behaviour change techniques (BCTs) used specifically in home-based cardiac rehabilitation programmes. I also wanted to try to appraise their effectiveness in reducing cardiovascular disease risk factors. The information from this systematic review of the literature as well as the information from the previous Chapter was used in the initial development of '*The Healthy Brain Rehabilitation Manual*'.

Objectives

To identify and describe the use of BCTs in home-based cardiac rehabilitation programmes and appraise their effectiveness in reducing cardiovascular disease risk factors.

Introduction

Cardiovascular diseases (CVD) are one of the leading causes of death, with survivors often being left with considerable morbidity and disability (156). Cardiac rehabilitation (CR) is an effective form of secondary prevention for CVD patients, endorsed by international guidelines (120)(157)(158). CR is a complex health service intervention that uses BCTs to assist patients to improve adherence to health-related behaviours in order to effect changes in different modifiable vascular risk factors. According to the MRC guidelines (127)(159), the application of behaviour change

theory is required in order to understand the interaction between patients and their use of complex health service interventions (86).

Guidance on individual-level behaviour change interventions for promoting change in modifiable cardiovascular risk factors (136) has indicated that the three behavioural change areas that are associated most positively with change in modifiable vascular risk factors are: (1) goals and planning, (2) feedback and monitoring, and (3) social support. These areas correspond to Michie's BCT taxonomy (128), which is an agreed list of 93 distinct labels to report the 'active ingredients' within a behaviour change intervention. This taxonomy (128) clusters individual BCTs into hierarchical groups that appear together commonly in behavioural interventions. Its use should allow more rigorous and precise reporting of the content of interventions, with better interpretation of outcomes.

There is strong evidence via a systematic review and meta-analysis (120) to support the use of CR programmes, including home-based approaches, in a patient population with cardiovascular disease, particularly for patients who have suffered a myocardial infarction. Audit data do not differentiate home-based programmes from those delivered in other settings but indicate that whilst only approximately 45% of those invited participated, almost 80,000 patients received CR in the UK in 2014 (160). Reasons for non-participation include problems with transport and a dislike of group rehabilitation: adherence is better with home-based than hospital or centre-based programmes (161). However, despite the evidence for this positive treatment option for vascular secondary prevention, there is not a clear understanding about how this complex health service intervention influences modifiable CV risk factor behaviours. This review, therefore, aimed to identify the BCTs which have been used in home-

based CR programmes and to describe the frequency of their use in relation to programme effectiveness in reducing CVD risk factors.

There has been little focus on the use of specific BCTs, particularly within secondary prevention programmes in the setting of a patient's home. An understanding of which BCTs have been utilised in interventions, will allow a more accurate replication and implementation of them within clinical practice and in research. Understanding which BCTs are used allows also an exploration of causal pathways, thereby facilitating intervention refinement by, for example, removing programme content that is not working and improving further aspects that are functioning well. This systematic review was designed to identify associations between particular BCTs and improvements in specific modifiable cardiovascular risk factors; and to contribute to the further development and refinement of home-based rehabilitation interventions for CVD patients.

Methods

The protocol for this review was previously published (162) and the Behaviour Change Taxonomy v1 (128) was used to identify the specific BCTs used within included studies. The lead authors attended a training workshop by the taxonomy's developers and one author (MAT) is a recognised 'expert coder'.

This systematic review is reported in line with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidance (163)(164). Key criteria for considering studies for inclusion included randomised and quasi-randomised controlled trials of home-based CR programmes initiated following a cardiovascular

event, e.g. post-myocardial infarction or following a heart failure exacerbation, published between 2005 and 2015. The publication period 2005 – 2015 was chosen to provide an up-to-date review on the effectiveness of cardiac rehabilitation for cardiovascular patients despite improvements in medical and surgical care, for example use of angioplasty for myocardial infarction patients. The review focused on adults, males and females, aged 18 years or older. Any CR programme, defined by previous authors (120) as "a structured programme, with clear objectives for the participants, including monitoring, follow-up, visits, letters, telephone calls from staff, or at least self monitoring diaries", which was a comprehensive biopsychosocial intervention aimed at targeting traditional risk factors for CVD, delivered within the home environment, initiated following a cardiovascular event, was eligible for inclusion. Studies that reviewed, for example, only an exercise or training programme for the patient were excluded. Trials with a control group and trials with multiple intervention arms (comparing different types of rehabilitation interventions) were included but the review did not include population or community-wide interventions.

Types of outcome measures

We identified and classified, using Michie's Taxonomy, the particular BCTs that were used in home-based CR programmes for cardiovascular secondary prevention. In addition, we assessed the frequency of use of BCTs in programmes that reported reductions in CVD risk factors. A meta-analysis of differences in effect between home-based and comparator programmes in relation to CVD risk factor outcomes illuminated key BCTs.

Search methods for identification of studies

Detailed search strategies were developed for each electronic database searched including Ovid MEDLINE(R) 1946 to June 2015, Ovid Embase 1974 to June 2015, EBSCO Cumulative Index to Nursing and Allied Health Literature (CINAHL) plus 1937 to June 2015, Cochrane Database and Ovid PsycINFO 1806 to June 2015. The searches were based on the strategy developed for Medical Literature Analysis and Retrieval System Online (MEDLINE) (**Appendix III**) and revised appropriately.

The titles and abstracts of publications obtained by the search strategy were independently screened by two authors (NH 100%, MEC 100%). Articles that did not meet the inclusion criteria were removed. All remaining publications were retrieved for further assessment. One supervisor and I independently (NH, MEC) selected the trials eligible for inclusion in the review with, if necessary, a second supervisor (FK) resolving disagreements. A record was kept of all articles excluded at this stage and the reason for their exclusion. No language restrictions were made. Additional studies were also identified from reviewing the reference lists of the retrieved papers through a hand search.

Data on methodological issues, eligibility criteria, BCTs (128), interventions (including the number of participants treated and intervention provider) and study design, study duration, follow-up, comparisons, outcome measures, results, withdrawals and adverse events were extracted independently by myself and one supervisor (NH, MEC) (**Table 3**). There was no blinding to study author, institution or journal.

Assessment of quality and risk of bias

The PEDrO scale (140) (**Table 3**) was used to assess the quality of included papers in the review. In addition, I and one supervisor (NH, MEC) independently assessed each included study for risk of bias ('high', 'low' or 'uncertain') using the risk of bias tool, following guidance from the Cochrane Handbook of Systematic Reviews of Interventions (141), a second supervisor (FK) acting as arbitrator as required.

Measures of treatment effect

For each study, relative risk and 95% confidence intervals were calculated for dichotomous outcomes and mean differences and 95% confidence intervals were calculated for continuous outcomes. Where continuous outcomes were pooled on different scales, standardised mean differences were used. Where available, changes from baseline (mean change scores) were used in preference to follow-up scores. When combining results for the individual studies, I generally used mean differences and a random effects model due to the clinical variation within studies.

Assessing for heterogeneity

Diversity across the studies was assessed qualitatively in terms of the intervention (content, duration, frequency, provider and setting), participant demographic characteristics, outcome measures and follow-up. If two or more studies were considered clinically homogenous according to the above terms, data were assessed for statistical heterogeneity using RevMan version 5.1. The chi-squared ($\chi 2$) test was used in conjunction with the I^2 statistic, which describes the percentage of variability

in effect estimates due to heterogeneity. The level of significance for the $\chi 2$ was set at $p < 0.1$.

Data synthesis

Careful consideration was given to the appropriateness of conducting a meta-analysis. Data were summarised statistically when the data were available, sufficiently similar and of sufficient quality and the statistical analysis was performed in accordance with guidelines (141).

Behaviour change techniques (BCTs)

I and another trained reviewer (NH, MAT) independently screened included articles and extracted BCTs using Michie's BCT taxonomy (128).

Results

The search criteria returned 2,448 articles and the full text articles of 31 papers was reviewed, identifying 24 possible studies for inclusion in this review (**Figure 5**). From a hand search of the reference lists of the 24 studies, 6 additional potentially eligible studies were identified. Eleven studies were included in the final review; of the 19 excluded, 10 were excluded because there was no randomisation, 7 were excluded as they did not assess a home-based CR programme and 2 were excluded as there was no appropriate outcome measure.

Programme design and evaluation

Of the 11 studies included, 4 used the 'Heart Manual' as their home-based CR programme (114)(165)(166)(167). Three used technology to assist delivery of the home-based CR intervention, including a smartphone (168), the internet (169) and telemonitoring (170). In the remaining 4 studies CR was delivered in the participant's home by physiotherapists (171)(172) or nurses (173)(174).

In 7 studies the control group was hospital- or centre-based CR (114)(166)(167)(168)(170)(173) whilst in 2 studies the control groups received 'usual care' (165)(174) and in 2 they received no active treatment (169)(172) (**Table 3)**. One study was conducted in each of the following countries: Canada (169), Australia (168), Poland (170), Norway (174) and China (165); 2 were conducted in Denmark (171)(172), and 4 in England (114)(166)(167)(173).

In 10 studies, patients were post-MI or post-angioplasty/CABG and one study included exclusively patients with heart failure (170). All participants were recruited from secondary care. Outcomes were assessed from 8 weeks (170) to 1 year (114)(171)(172).

Quality and risk of bias

Using the PEDrO scale (140) (**see Table 4**), all included studies were deemed to be of high methodological quality. All were randomised controlled trials with a low risk of bias (141). The study by Dalal et al, 2007 (166) also had a patient-preference arm so that only data for the randomised patients were included in the meta-analysis. Jolly et al, 2009 (114) and Lee et al, 2006 (167) were the only two studies that had blinding of

assessors to the outcome measures. Study follow-up overall varied from 77% (168) to 100% (167)(172) and all studies accounted fully for study participants and provided reasons for any missing data. No other potential sources of bias were identified.

Assessment of reporting bias

Funnel plots were produced to assess reporting bias and no obvious reporting bias was found as illustrated in **Figures 6** and **7** in respect of systolic blood pressure and diastolic blood pressure outcomes.

Effects of interventions

All but one study (174) reported a positive effect for home-based CR on modifiable CVD risk factors. Combined outcome data from all types of comparator groups in the included studies were used to compare the effectiveness of home-based and comparator programmes. For both Oerkild et al studies (171)(172) the data at the three month review, which reported the change from baseline, were used for meta-analysis and in the study by Dalal et al (166) only randomised study data were used.

A meta-analysis was undertaken on 8 individual variables to compare outcomes between home-based and comparator programmes in the included studies. There was no significant difference between home- and hospital centre-based CR on resting systolic blood pressure (1.02mmHg, 95% CI -1.74 to 3.78, p-value = 0.3) (**Figure 8**), resting diastolic blood pressure (-0.89mmHg, 95% CI -4.35 to 2.58, p-value = 0.62), peak VO_{2max} (1.19 ml/kg/min, 95% CI -0.78 to 3.16 p-value = 0.24) and the distance covered in the six-minute walk test (8.47m, 95% CI -10.98 to 27.92, p-value = 0.39).

There was also no significant difference between home- and hospital-/centre-based CR in terms of overall treatment effect for total cholesterol (0.07mmol/l, -0.16 - 0.29, p-value = 0.56) (**Figure 9**), HDL-cholesterol (0.01mmol/l, 95% CI -0.06 to 0.07, p-value = 0.79), and LDL-cholesterol (0.02mmol/l, 95% CI -0.25 to 0.29, p-value 0.88) or for the anxiety (0.02, -1.29 to 1.32, p-value = 0.98) (**Figure 10**) and the depression sections of the HADs questionnaire (-0.21, -0.74 to 0.32, p-value = 0.44).

Behaviour Change Techniques in Included Studies

It was not possible to compare the relative effectiveness of different BCTs or to conduct a meta-regression of the BCTs as only a limited number of studies had comparable outcome data (141). The BCT identified as 'social support (unspecified)' was employed in all 11 studies whilst the BCT 'goal setting (behaviour)' was employed in 10 studies (**Table 4**). The 'Heart Manual' intervention utilised the BCTs of goal setting (behaviour), monitoring of behaviour by others without feedback, self-monitoring of behaviour, self-monitoring of outcome(s) of behaviour, social support (unspecified), instruction on how to perform the behaviour, pharmacological support and reducing negative emotions. All studies except one (174) reported significant positive effects in change of measured CVD risk factors: the BCTs which were not utilised in Lie et al (174) but were generally included in other successful programmes included those related to monitoring, instruction on how to perform the behaviour and credible source. The BCTs that were employed in this study (174) were social support, goal setting, reducing negative emotions, pharmacological support, information about health and problem solving.

The commonest group of BCTs used in the 11 included studies was 'feedback and monitoring', whilst the second most common group utilised was 'social support'. Of all the groups of BCTs listed in the taxonomy (128), 6 were not identified as having been used within any of the studies: these were 'associations', 'reward and threat', 'identity', 'scheduled consequences', 'self belief' and 'covert learning'.

Discussion

Summary

This systematic review comprised 11 randomised controlled studies of home-based CR programmes for CVD patients with comparator programmes, the majority of which were centre- or hospital-based CR. This is the first review to identify, collate and analyse observations regarding the use of BCTs within home-based CR programmes, including the Heart Manual. A wide range of different BCTs were used in the included studies, with 'social support (unspecified)', 'goal setting (behaviour)', monitoring, instruction on how to perform the behaviour and credible source being used commonly in effective programmes. The 'Heart Manual' intervention utilised these BCTs, as well as 'pharmacological support' and 'reduce negative emotions', and was consistently effective in modifying CVD risk factors in the included studies.

Comparison with existing literature

Previous studies have highlighted the comparable effects of home-based CR and hospital-based programmes (120)(175)(176). This study supports these findings by illustrating in the meta-analysis that home-based CR provides comparable

improvements in CVD risk factors to other treatment options, including hospital-based approaches. Indeed all but one study illustrated the positive effect of home-based CR on modifiable CVD risk factors. My study adds to previous findings by including a wider range of cardiovascular patients, including heart failure and post-coronary vascularisation patients and programmes delivered utilising latest technology (e.g. smartphones), which were not included in previous reviews (120). Also, it includes more recent publications (from 2005-2015) than were included in previous reviews (120)(175)(176), which therefore has relevance to current medical management. Home-based CR programmes are attractive to patients due to their accessibility (120)(176) that helps to improve compliance (121). Also, they tend to be less costly than hospital- or centre-based programmes (121) and fit with the aim of shifting patient management from a hospital base, into the community – a current theme within modern healthcare (177).

Guidance on individual-level behaviour change interventions for promoting change in modifiable cardiovascular risk factors in the public (136) recommends that these programmes should include support for individuals to make change through self-monitoring, goal setting, social support and relapse prevention strategies and the provision of relevant information on the health consequences of the behaviour. The findings in this review are in keeping with these guidelines: the BCT 'social support (unspecified)' was employed in all effective studies included in this review and the BCT 'goal setting (behaviour)' was utilised in all but one (169). Few studies utilised self-monitoring and relapse prevention strategies. Indeed only 6 studies (114)(165)(166)(167)(168)(169) utilised the BCTs of 'self-monitoring of behaviour' and 'self-monitoring of outcome(s) of behaviour'. Within the taxonomy (128) there is no specific BCT for relapse prevention but this could be covered by other BCTs such

as ‘action planning’. Future studies aimed at developing home-based CR programmes for cardiovascular patients should consider how best to use these techniques (self-monitoring, goal setting, social support and relapse prevention strategies), to maximise the likelihood of establishing and maintaining new behaviours to optimise secondary CVD prevention. In particular, self-monitoring and relapse prevention strategies should be further developed and their impact assessed on tackling modifiable CVD risk factors.

Limitations and strengths

I have attempted to identify all studies of potential relevance by developing a comprehensive search strategy and supporting this through hand searching reference lists of all full text articles assessed for inclusion in the review. Visual inspection of funnel plots provided little evidence of publication bias. All eligible studies, regardless of publication language, were included.

A limitation of this review is that included studies lacked consistency in the outcome measures used and follow-up duration varied from 8 weeks to one year, so that combining results in a meta-analysis was difficult. Shorter follow-up durations may not allow sufficient time for interventions to produce an impact on modifiable vascular risk factors and early changes may not be sustained. Intervention intensity was also different across the included studies and could be a potential source of bias within the review. Further studies should compare and contrast the use of BCTs within home-based CR compared to programmes delivered in other settings.

Conclusions

This review offers new understanding about some of the key features that characterise effective home-based CR programmes. The BCTs of 'social support (unspecified)' and 'goal setting (behaviour)' were frequently found as components within programmes that showed a reduction in CVD risk factors. Failing to provide a credible source or instruction on how to perform a behaviour was linked with lack of effectiveness. Thus, the likelihood of delivering a beneficial CR programme appears to be enhanced when patients are supported by family, friends and patient-peers to engage and persist with the programme; facilitated to set goals regarding lifestyle behaviours; given professional feedback via ongoing monitoring; and taught or trained to execute or change specific behaviours. However, further robust trials that describe and evaluate the use of different BCTs (128), building on NICE guidance (136), are required in order to refine the design of home-based CR programmes for *optimal* secondary cardiovascular disease prevention. These study findings have been used to refine '*The Healthy Brain Rehabilitation Manual*' for my initial feasibility study.

Chapter 4

Patients', health professionals' and academics' views regarding '*The Healthy Brain Rehabilitation Manual*', version 1, and its use in the TIA and 'minor' stroke population

Aim

To test and refine version 1 of '*The Healthy Brain Rehabilitation Manual*' for people who experience a TIA and 'minor' stroke (139)(162)(178)(179).

Objectives

To elicit patients', carers', health professionals' and academics' views about the initial version of '*The Healthy Brain Rehabilitation Manual*' for use in the acute period following a first TIA and 'minor' stroke of atherosclerotic origin. In particular, a key objective was to capture views about the usability, accuracy and helpfulness of the manual.

Method

I completed systematic reviews (SRs) of relevant literature (as detailed in Chapters 2 and 3) and then used the results from the SRs to adapt the 'Heart Manual' (180)(181) for the TIA and 'minor' stroke population. The 'Heart Manual' was chosen as it is well evidenced for secondary cardiovascular prevention (122)(166) though it has never been used with cerebrovascular patients, despite these conditions sharing similar underlying risk factors and pathology.

This first draft of '*The Healthy Brain Rehabilitation Manual*' (**Appendix IV**) was appraised by analysing the data from 3 focus groups (FG) consisting of 4 patients and 1 carer (FG 1), 9 health professionals (FG 2) and 4 public health intervention researchers (FG 3). Participants were emailed an electronic version of the manual

approximately 2 weeks before the interview to allow them time to review the manual. They were also given a paper copy of the manual approximately 30 minutes before starting the focus group. The topic guide for the focus group discussions is included within **Appendix V** and no repeat interviews were carried out. Field notes were made during and immediately after the focus groups were conducted.

The focus group participants for focus groups 1 and 2 were recruited through opportunistic sampling whilst focus group 3 participants were purposively selected for their clinical and research experience. The participants in the first focus group were recruited through the Chest, Heart and Stroke (NI) charity (1 female and 3 male patients (1 post-TIA; 3 post-'minor' stroke) and one female carer), with an age range from 29 to 76 years old. The participants were contacted by the charity on my behalf and were asked to attend the charity headquarters on a certain date for the focus group. All 5 participants (4 patients and 1 carer) who were contacted by the charity agreed to attend the focus group. Meanwhile all health professionals who worked within an acute stroke unit in one of the recruiting hospitals for the pilot study were invited to attend the focus group via an open letter from the researcher. This focus group of hospital professionals was held for convenience during a lunchtime period in the hospital on the stroke ward. It comprised 9 health professionals, all females, including 3 stroke nurses, 2 physiotherapists and one each of the following: a stroke consultant, a pharmacist, an occupational therapist and a speech and language therapist. The age range of this group was 31 to 58 years old. The participants in both these focus groups did not have any previous relationship with the interviewer.

A third focus group comprised public health intervention researchers from the Centre for Public Health, Queen's University Belfast. The 4 individuals were selected purposively because of their experience in intervention and service development and

their varied disciplinary backgrounds: 1 female and 3 males, including a General Practitioner, a social scientist-social worker, a public health medicine consultant and epidemiologist and a health services researcher-health psychologist. The age range of these participants was 30 to 63 years old. These individuals were also selected because of their knowledge and experience of working with TIA patients, stroke services and preventative medicine and health care. These focus group participants had a professional, working relationship with the interviewer, NH. Each group was informed that the purpose of the focus group discussions was to appraise the initial version of '*The Healthy Brain Rehabilitation Manual*' and to further refine it.

Each focus group discussion was audio-recorded with the consent of study participants and lasted approximately one hour. The researcher, NH, led each focus group and there was a topic guide to direct the discussion. The interviewer, NH, undertook a non-scheduled standardised focus group approach (182) with all 3 groups and the focus group discussions were transcribed from audio recordings by the researcher, NH. A content analysis with the practical purpose of eliciting views about the acceptability and usability of the intervention or programme manual was conducted and how the manual could be further refined. A male GP, NH, and a male health services researcher/health psychologist, MD, read and reread the transcripts and coded the content independently. NH and MD met to discuss the transcripts and agree the main areas covered within the transcripts. MC, a female professor of GP, acted as a referee as required as well as appraising critically the categories and the degree to which the transcript extracts and quotations supported the themes. The transcripts were not returned to participants for comment and/or correction and participants were not asked to provide feedback on the qualitative results. NH has basic training in qualitative research methods whilst MD and MC are relatively experienced qualitative

researchers. The independent results of the qualitative analysis and data interpretation were discussed with the entire research team, to ensure clear definition of themes and that appropriate supporting evidence was identified for each. The reporting of this qualitative study and findings followed the guidance set out in Murphy et al (182) and other authors (183) as well as the COREQ checklist (184).

Results

As noted above, the practical purpose and focus of this interrelated component of the PhD research project was to elicit views about the acceptability and usability of the '*The Healthy Brain Rehabilitation Manual'* and how it might be improved. Four over-arching areas emerged from the focus group analysis, all of which were discussed to some extent in the all 3 FGs:

- **Manual format and content;**
- **Information to be added to the manual;**
- **Items to be omitted from the manual; and**
- **Use of the manual.**

Each focus group focused on an area particular to their group as well as covering the same general areas. Indeed, the patient focus group tended to focus on the impact of diagnosis, the health professional group gave greater emphasis to the content of the manual and the academic focus group enquired about and discussed supporting evidence for the manual. The results of the focus groups are discussed collectively, mindful of the aims and objectives of this part of the PhD investigation. In order to preserve anonymity, quotes are presented with a participant's age and sex.

1: Manual format and content

a) Format

The front cover of the manual was well received by patients and appeared to help people want to engage with the manual. The general view from the FGs was that the manual was very readable, with content appropriate to the target level of readership, though a readability score was suggested to be undertaken to support these subjective feelings.

> "*I think it's really good. Most of the other front covers would put you off reading their material but that makes me want to read that.*" *(29yo, female)*

> "*I thought it was comprehensive but not over-bearing, not over-powering.*" *(57yo, male)*

> "*I found the practical tips and the stress section very easy to follow. With the exercises, they are things you could do in the house and you don't need any equipment – I think that's what you need – I think that's what you'd want as a health professional and service user.*" *(30yo, male)*

b) Content

The manual content was generally well received, with the medication chapter, Section 5, particularly well received and, according to patients, the knowledge that they acquired through reading and using the manual helped them to engage in appropriate conversations with their health professionals:

"I thought it (the manual) covered everything, very comprehensive." (76yo, male)

"*I thought it (Section 5) gave just enough information….it covered all the general ones (medication) which are used and gave you points to talk to your doctor about….*" *(52yo, female)*

The smoking section was also well received by patients who appreciated the practical advice with regards smoking cessation:

"*I think the section on smoking is very useful. I'm an ex-smoker and I would have used most of the hints in the book to help me stop. The hints are very good, to get you out of the habit of smoking*." *(52yo, female)*

Participants reported that they enjoyed the diary and the section in the manual in which they were requested to write down questions or points of information. They also appreciated the section on sexual health and relationships and commented that most health professionals tended to avoid discussing this aspect of health and rehabilitation:

"*the wee diary is very good, to write things down…" (52yo, female)*

"*I think that was a good section (sexual health) to have because no one ever said anything about it…" (52yo, female)*

"*I think it's good because a lot of people would have issues around this (sexual issues) and would be too scared to talk about it…*" *(42yo, female)*

The practical advice included in the diet section was also well received by patients, with people making positive behaviour changes due to the information contained

within the manual and the health professionals felt that the knowledge contained within the manual could support them to do their job:

> "*I've started eating an apple, a banana and a pear everyday…*" *(76yo, male)*

> "*For me working as a social worker in the community, I would find it (the manual) very useful. I thought the practical tips were very good and I don't think as a healthcare professional, that it would take up too much of my time…*" *(30yo, male)*

Anxiety and stress were viewed as a significant cause of strokes by patients, with patients being positive about how the manual managed these symptoms by providing appropriate information:

> "*I was doing my finals and I was completely stressed out. I think that they don't know what caused my stroke but to this day I think it was the stress and that I put too much pressure on myself.…..Yes, stress was a big thing for me…The book is brilliant in explaining that*." *(29yo, female)*

Inclusion of information about post-TIA and post-stroke fatigue was welcomed. These symptoms had a big impact on patients and this was compounded by the lack of knowledge about these conditions by health professionals. Someone also commented that when they mentioned fatigue/tiredness to their health professional, they were 'made to feel' that they were fabricating their symptoms:

> "*That's the thing I can't take, the tiredness, I just can't take it….*" *(57yo, male)*

> "*I went to a locum (GP) and was telling him about the tiredness and fatigue and he told me that fatigue and tiredness has nothing to do with the stroke. I just got up and left, I didn't even want to speak with him." (49yo, male)*

> "*when P goes to the doctor, he is made to feel that he is over anxious, that he is imagining these things and he's not*." *(52yo, female)*

Employment information following the event was clearly important to patients and patients generally agreed that there was confusion about the length of time to take off work following the event:

> "*I would just like to add about going back to work, that I was given a lot of mixed messages – some people were like give it a couple of months, others were like a couple of weeks…others said 6 months…That's the question, when should you go back to work?..... I was never told how long." (29yo, female)*

The academic group were also keen to know the evidence-base for the content of the manual and that appropriate resources had been consulted when compiling the manual. For example:

> "…..*have you taken most of this information from the current smoking cessation services?" (57yo, male)*

They also commented about moving the section on general information about TIA and strokes from the back of the manual to the front:

> "*I would move that general information section at the end to the beginning so people know what they have and what has happened to them…*" *(58yo, female)*

2: Information to be added to the manual

Health professionals were keen for people to be made aware of existing exercise and health advice classes in the community, e.g. the Chest Heart and Stroke (NI) Post-rehab Exercise Programme (PREP) exercise classes and the 'Healthwise' GP referral schemes. They also wanted a section in the manual where they, as health professionals, could write down information for the patient and questions for the patient to ask other health professionals, supporting the home exercises with simple diagrams to make them easier to understand was suggested. Patients also felt unsure about how much exercise and physical activity to do. One patient in particular wanted to know when he was able to start running after a TIA or stroke and requested further information be added to the physical activity and exercise section of the booklet. Academics also suggested using more lay language for the alcohol section.

> "*On the physical activity section, I would include a section on a diary so that people can write down their goals and plans and record what they are doing…*" *(46yo, female).*
>
> "*they really need to keep their own diary and put in it how much physical activity they are doing…." (57yo, male)*
>
> "*I would have a section for health professionals to write advice on….*" *(42yo, female)*
>
> "*I found the heel dig exercises difficult to follow…and a bicep curl – I don't think the lay public will cotton onto that….*" *(63yo, female)*
>
> "*…he just doesn't know how much exercise he should do…*" *(52yo, female)*

"I would have brackets 'small glass' when describing what a unit of wine is." (57yo, male)

Health professionals were also keen that cholesterol as a cardiovascular risk factor be discussed in greater detail and the need to take statins life-long, regardless of their cholesterol level, with the manual being developed into different formats, for example, 'an app'. To support the dietary information, it was suggested to add further detail on how to increase olive oil consumption and to include contingency plans within the manual to help prevent relapses:

"*What about discussing cholesterol and telling them about that. I think it is something which people generally struggle with understanding*." *(42yo, female, 2)*

"*Could they have an app (version of the manual)*?" *(42yo, female)*

"*…give people practical tips on increasing their olive oil consumption, e.g. use it over your potatoes instead of butter, etc*". *(57yo, male)*

"*the other technique which applies to most of these sections is a writing of a 'if when plan'. For example, if I feel hungry, take low sugar chewing gum…*" *(57yo, male)*

The health professionals also felt that more information was required relating to fatigue and mood disturbance post-TIA and stroke, reporting that it causes significant issues for patients post-TIA/'minor' stroke and that it could be treated with 'energy conservation' techniques, particularly as symptoms might be prolonged:

"*I think it's good that you have tried to tackle this (fatigue and mental health issues) but one of the big things which is lacking for people after a TIA or stroke is psychological support*." *(42yo, female)*

"*I think post-stroke fatigue really frightens people. People describe it as overwhelming – like someone has just pulled out their energy source…. (42yo, female)*

"*I would highlight to people that stroke fatigue is different from normal fatigue – this is not something which gets better with rest and sleep….I would highlight energy conservation techniques to them – how to do things in a certain manner to conserve energy*." *(37yo, female)*

"*The important thing to tell patients as well is that it is not always something which goes away or gets better but that it is about managing it…it also makes them feel more normal knowing that it might not get better….*" *(37yo, female)*

The health professionals felt it was better to educate patients about managing the fatigue symptoms when they were back in the community and able to assess what impact the fatigue symptoms were having on their lives, rather than in the acute hospital setting. The health professionals were also aware of the non-visible signs of this condition and need for a recovery period following the cerebrovascular incident:

"*Sometimes it is also not best to discuss this (fatigue) in the ward but better discussed in the community when they are back into their routine and they see what an impact it is making on their life….*" *(37yo, female)*

"*I think they (patients) forget that because they don't have a visible scar, like an operation, that their brain has a scar, that their nervous system is*

recovering and that this will take time to recover just the same as a physical scar would heal." *(42yo, female)*

Patients asked for more information about the potential side-effects of medication, though they acknowledged that such information might make them less likely to comply with their medication regimes. They also thought it was important to let people know that they might only get visual symptoms as part of their TIA and stroke, which is not currently included within the UK public health FAST campaign (185). One patient thought that visual symptoms should be included in the manual for alerting patients to the fact that they may be having a TIA or stroke:

"*I think that (vision) is something you should put in the booklet so people are aware of it*." *(29yo, female patient)*

3: Items to be omitted from the manual

The health professionals did not want 'thrombolysis' included within section 5, the medication section, because they felt that if patients did not receive it, then they would view this negatively:

"*no (don't include a thrombolysis section) because if they don't get it then people will be saying, 'why didn't I get that?'….It is discussed in hospital if they get it*." *(42yo, female)*

They also did not want home blood pressure (BP) monitoring devices included in the manual as they felt it caused unwarranted anxiety for the patient:

"*I would generally discourage people from using home BP monitors*." *(37yo, female, health professional).*

Neither of these points was raised in the other 2 FGs. It was also suggested to reduce the size of section 3 relating to diet and to include the title of each chapter with numbering for each manual section.

"*I felt it (Section 3) was a bit repetitive in places – I think you could cut it down…*" *(58yo, female)*

"I would add the section headings to the numbering throughout the book so it's easier to follow." (30yo, male)

4: Use of the manual

a) Facilitator

The academic group viewed the manual facilitator as an important tool for the success of the intervention:

"*So I wouldn't underestimate the facilitator's role – I think this is the key mechanism for effecting change*." *(46yo, male)*

There was also some discussion about who was best placed to be the facilitator – GP, stroke nurse or peer and it was suggested to try to tease this out within the pilot study through appropriate group comparisons although no mention was made of contact frequency.

b) Timing

Patients thought that the most appropriate time to receive the manual would be near or around the point of discharge or when they were leaving the hospital after they had received their diagnosis:

> *"I was just going to say that when I was discharged from hospital, something like this would have been fantastic….It's great to just let people know, to just be more aware (of TIA and stroke symptoms)." (29yo, female)*

c) Target Audience

Patients also considered that the manual could be used for a wider audience. They wanted the general public, particularly children and younger adults, to be educated about the causes and consequences of strokes. This education was seen as particularly key because family members and carers were viewed as important in spotting the diagnosis and ensuring they receive appropriate treatment:

> "*I would love to see people getting into schools and advising people about stress, especially in the run up to exams and educating them about TIAs and strokes…" (57yo, male)*
>
> *"I collapsed in the bathroom and the wife was there, otherwise I wouldn't have known what would have happened to me…she saw the signs straight away and got straight onto the ambulance and they then talked her through everything…" (76yo, male)*

Discussion

Collectively, the focus groups were successful in terms of providing critical feedback about the initial version of '*The Healthy Brain Rehabilitation Manual*', adapted from the 'Heart Manual' (111). I used the results of the analysis of the focus groups' data to refine and adapt the manual for use in the acute period following a first TIA and 'minor' stroke of atherosclerotic origin. The main areas of discussion within these focus groups were manual format and content; information to be added to the manual; items to be omitted from the manual; and use of the manual. The manual was well received by all groups, particularly in terms of managing mental health symptoms and tackling potentially embarrassing topics, e.g. discussions around sexual health. Perceived benefits of the manual included increasing knowledge about the condition and that it facilitated family involvement in the rehabilitation process. The facilitator was viewed as a key delivery mechanism for the manual and the main suggestions to improve the manual included making the home exercise sections easier to follow for patients. Particular post-event issues that the patients identified were returning to work and the impact that the diagnosis had on employment, how much physical activity to do and managing fatigue and mood symptoms. Another issue for patients was that the consequences following the TIA or 'minor' stroke were often not visible to others and they therefore felt it was difficult to justify, e.g. absences from work.

Post-TIA/stroke fatigue and mental health issues

Fatigue is common after both TIA (186) and 'minor' stroke although it is more common following a stroke – being reported to occur in 29% of post-TIA patients with an incidence of 56% in stroke patients (134). Fatigue interferes with a patient's

rehabilitation potential and is an independent predictor of post-stroke disability and level of care (187). Thus this is an important area that is currently being inadequately managed for these patients. Although there are no definitive treatment options for this challenging symptom, there are different treatment options which could be helpful (188)(189) and which can be promoted within the manual and by the facilitator. These options could include graded exercise and cognitive behavioural approaches as well as pharmacological approaches. Anxiety and depression are also common post-TIA and stroke (190). These psychological symptoms can overlap with the fatigue diagnosis and are often treated in a similar fashion.

Health Literacy

Participants were keen to engage and find out further information about TIAs and strokes and their future health risks, helping to improve their health literacy, which is supported by other authors (186)(191)(192). Patient engagement was helped by the manual having a readability score of 13 to 14 year olds (http://www.webpagefx.com/tools/read-able/check.php) and this assessment was undertaken following the comments from the focus group of academics. Indeed a Cochrane review (193) highlighted the fact that stroke survivors and caregivers are keen to engage in information exchange with service providers and that this improves their knowledge of cerebrovascular conditions, improves satisfaction with the services offered and reduces patient depression scores. This is important as research has highlighted the direct association between low levels of health literacy and poor health outcomes (194)(195), with patients with low health literacy less likely to ask questions of health professionals and engage in shared decision making with the health

professional caring for them (196). However improving health literacy can potentially have negative consequences, including increasing health anxiety amongst patients through inappropriate Internet searches (197), which can be overcome by having repeated contacts with the patient as well as appropriate communication skills.

Focus group participants generally felt that there was not enough knowledge in the general population about TIAs and strokes and this is in keeping with previous studies, highlighting that knowledge of cerebrovascular disease in the general population is poor (191)(198). Patients wanted to particularly highlight to the general population that TIAs and strokes do not just affect older people, also affecting younger members of the population, with one stroke survivor in the patient focus group, for example, being 29 years old. Patients also felt it was important to emphasise that when you experience a TIA or stroke, people might only experience visual symptoms and not just the traditional face, arm and speech symptoms promoted within the UK FAST public health campaign (185). Patients therefore wanted the public to know about and to act on these symptoms and to not simply ignore them, through appropriate public health campaigns and through promoting use of the manual.

Social impacts following a TIA/minor stroke

As well as the physical and psychological consequences following a TIA or 'minor' stroke, there are also social implications, with patients reporting that the diagnosis impacts on their ability to drive, employment and obtaining insurance (e.g. travel insurance) (186). Patients also found it difficult to adopt the 'sick role' (199), as there was often no outward physical sign of illness following the TIA or 'minor' stroke. Indeed this often manifested itself in patients being unsure about how much time to

take off from work as well as a feeling by patients that people in their work would be thinking that they were taking too much time off. Previous authors (200) have reported that this makes the patient feel like a "fraud". Moreover, these authors commented that the main reason for people taking time off from work following a TIA was due to non-visible impairments and that a lack of understanding of these symptoms from their employer, often leads to difficulties for them in returning to and continuing in work (200). The commonest non-visible impairment reported was fatigue (200) although other common non-visible problems can include personality changes, pain and memory difficulties with employer 'support' viewed as important in allowing people to return to work. Moreover other authors (191) have commented that this lack of enduring physical signs of ill-health from a TIA or 'minor' stroke has resulted in patient non-compliance with medication although participants in this current study did not report this. Medication and treatment compliance is therefore important to emphasise to TIA and 'minor' stroke patients.

Improving intervention adherence and compliance

Patients generally enjoyed writing down goals in their rehabilitation manual and completing a diary as well as being able to talk to a health professional about these. Indeed a recent systematic review was conducted into exercise adherence in patients with mild cognitive impairment, which occurs in over a third of TIA patients (201), and found that exercise prescription adherence improved if it was individually tailored, sufficient information was provided to participants and phone calls, pedometers and exercise logs were used as well as supervision provided (202). These features are in keeping with the National Institute of Health and Care Excellence (NICE) guidance on

individual-level behaviour change interventions for promoting change in modifiable cardiovascular risk factors (136) and all these elements are included within '*The Healthy Brain Rehabilitation Manual*'. Furthermore, a recent Cochrane review has highlighted the effectiveness of self-management programmes, similar to '*The Healthy Brain Rehabilitation Manual*', in improving quality of life and self-efficacy for post-stroke patients (203). Health professionals also wanted 'if-then' plans (204) included within the manual so that patients could identify opportunities to act for their health and then the next steps to be taken in carrying out that good intention. Hospital health professionals cautioned against the use of home blood pressure monitoring within the manual. This is contrary to a recent study published in the Lancet (205), which found that self-monitoring improved blood pressure management in primary care hypertension patients. Blood pressure is a key modifiable risk factor for stroke (34)(206) and I would therefore like to do further qualitative work on home blood pressure monitoring to understand its potential role within the intervention.

How the manual changed following the qualitative work

The content of the manual was adapted following the review and analysis of comments received from the patients, health professionals and academics. The changes included:

- Adding a blank section to allow patients to write down questions which they could ask health professionals at their next medical visit;
- Visual symptoms were added to the traditional UK FAST alert about TIA or stroke signs and symptoms at the start of the manual (185).

- Further information was included about physical activity and exercise advice in section 2 of the manual, with patients being 'signposted' to the Chest Heart and Stroke (NI) PREP exercise classes (https://nichs.org.uk/how-we-can-support-you/stroke-support/) as well as community available resources, e.g. Healthwise (http://www.publichealth.hscni.net/news/get-healthwise-new-year), which the GP could refer them to in the community. Further space within the manual was also created for the physical activity diary.
- Section 3 on diet was refined and reduced in size, with practical tips added to the dietary section to increase olive oil consumption.
- A general readability score was also undertaken (http://www.webpagefx.com/tools/read-able/check.php showing it to be readily understandable by 13 to 14 year olds).
- Section headings were included with numbering and the 'SPRITE' title was removed from the front cover of the manual, both based on general comments to the interviewer.
- The alcohol section was altered to include more user-friendly language with 'small glass of wine' added, replacing 'a unit of alcohol' based on some general comments received by the interviewer within the focus groups.

Strengths and Limitations

The strengths of this chapter of thesis are the diverse backgrounds of patients, carers, academics and health professionals that reviewed the manual. In particular, the health professional focus group had a range of professions involved in TIA and stroke patient management. More than one researcher then reviewed the focus group feedback

independently and the review adhered to specific recognised qualitative methods. The patient focus group was recruited through the NI Chest Heart and Stroke charity and these patients might therefore be more aware of TIA and stroke issues than the 'typical' general population patient, providing me with a high-level of qualitative information. I was the lone facilitator of each focus group and participants knew that I was a GP and the lead developer of '*The Healthy Brain Rehabilitation Manual*'. Ideally, someone independent of the intervention development process should have facilitated the focus groups in order to avoid the possibility of influencing participants unduly. However, I conducted the focus groups mindful of my position and of the role of reflexivity (182) in qualitative research. For example, I contributed only minimally to the focus group, generally only asking the pre-designed questions in the topic guide. Furthermore, the flow of conversation, interactive nature of discussion and content of the transcript suggested that my role as FG facilitator or moderator did not appear to impact significantly. .

Conclusions

'*The Healthy Brain Rehabilitation Manual*' was developed according to the MRC Guidelines for developing complex health service interventions (127). The preparation of the first draft of this manual was based upon best available evidence from systematic reviews of the literature (Chapters 2 and 3 of the thesis) and the design was modelled on the successfully trialled 'Heart Manual'. This chapter presented the results of a qualitative study of the views of patients, carers, academics and health professionals regarding the initial draft of the manual. In addition, the chapter sets out how the results from this qualitative research were used to produce a revised draft of

'*The Healthy Brain Rehabilitation Manual*'. The next stage in the developmental and testing process involved designing and conducting a feasibility study of the early implementation of the revised manual with patients following a TIA or 'minor' stroke.

Chapter 5

Stroke Prevention Rehabilitation Intervention Trial of Exercise (SPRITE) - A Feasibility Study

Introduction

Strokes and transient ischaemic attacks (TIAs) are highly prevalent conditions (1)(207), with these patients being at high risk of further vascular episodes post-event (8). Therefore, the immediate period after a TIA and 'minor' stroke is a crucial time to intervene to reduce the risk of future strokes and the impact that these conditions have on society.

Cardio- and cerebro-vascular disease share common underlying pathological mechanisms and risk factors, but cardiac rehabilitation for secondary prevention is only offered to patients in the UK with cardiovascular disease (108) and further research has been highlighted as required in assessing the impact of lifestyle interventions post-stroke and TIA (208). Physical inactivity is one of the most important recognised risk factors for cerebrovascular disease (33) and pedometers have been shown to be effective in promoting physical activity (209). Pedometers also appear feasible for use by patients with stroke (90)(91) and promote walking, which is one of the commonest forms of physical activity for older adults to engage in (210). Other research has shown that vascular risk factors should be addressed as quickly as possible following the initial vascular event (11) but no authors have previously assessed the feasibility of adapting a home-based cardiac rehabilitation programme, with or without an added pedometer intervention, for use within the TIA and 'minor' stroke population in the sub-acute period following diagnosis. With home-based approaches reported to improve compliance as well as uptake to the rehabilitation programme (121) and have shown longer-term sustainability of health benefits compared with hospital-based programmes (123).

Information about the 'active' ingredients, such as specific BCTs (128), used within comprehensive programmes, such as '*The Healthy Brain Rehabilitation Manual*', would facilitate their replication and the implementation of guidelines for good clinical practice (135)(136). Identifying behaviour change techniques (BCTs) used in different behaviour change programmes has also been identified as a national research priority (136). Thus '*The Healthy Brain Rehabilitation Manual*', adapted from the 'Heart Manual', is being developed following the MRC guidelines for developing complex health service interventions (127), to maximise secondary prevention post-TIA and/or minor stroke.

Aim

The aim of this study is to assess the feasibility of evaluating the effectiveness of a novel adapted home-based cardiac rehabilitation programme, '*The Healthy Brain Rehabilitation Manual*', with or without a pedometer intervention, initiated within 4 weeks of a first TIA or minor stroke of atherosclerotic origin. I aimed to assess rates of recruitment, completion of outcome measures and follow-up, to explore participants' views of the programme and research methods, and to identify the BCTs used within the programme. I also aimed to assess if patients preferred to use a pedometer or a Fitbit to support the physical activity section of the manual.

Objective

To: (1) determine if it is feasible to initiate '*The Healthy Brain Rehabilitation Manual*', with or without a pedometer, within 4 weeks of a patient suffering a first

TIA or ‘minor’ stroke;

(2) assess the patient acceptability of the intervention(s),

(3) identify the BCTs utilised within the manual, and

(4) determine what patients prefer to use to monitor their physical activity levels, a pedometer or a Fitbit.

Methods

Trial registration and Ethics Approval

The study was approved by the Office for Research Ethics Committees, Northern Ireland (REC reference 15/NI/0001, 21/09/2015) and registered (ClinicalTrials.gov, NCT02712385). CONSORT guidelines for reporting randomised feasibility trials (211) as well as National Institute of Health Research (NIHR) guidance for feasibility studies (212) and the PREPARE trial guide (213) have been used in this report.

Study Setting and participants

Patients attending one TIA/ ‘minor’ stroke assessment unit at the Ulster hospital in Belfast (UK) were given information about the study by a nurse and asked for their consent to be telephoned by the lead researcher (NH) the following day to invite their participation. Those who agreed attended the Northern Ireland Clinical Research Facility (NICRF), Belfast City Hospital, for an initial meeting where, with consent, baseline data were collected.

Patients were eligible for inclusion if they were aged 18 years or older and within 4 weeks of their first symptoms of a TIA or 'mild' stroke. The diagnosis was made by the consultant at the clinic, based on history, neurological examination and neuroimaging (17). Using the TOAST classification system (214)(215) only TIAs and 'minor' strokes attributed to atherosclerosis or small vessel occlusion were included. Excluded patients were those who had unstable cardiac conditions or contraindications for exercise training (216), were unable to give informed consent or had a previous cerebrovascular event.

Data collection

At their initial meeting, lasting approximately one hour, the researcher measured height and weight (in light clothing, using a Seca scale, model 799), waist circumference (as per (217)), resting blood pressure and heart rate (using BpTRU, model BPM-200 (218), checked the heart rhythm manually to exclude any dysrhythmias (radial pulse for 1 minute) and recorded other variables including sex, age, marital status, smoking status, alcohol intake (units in a typical week before diagnosis), time from initial event to study enrolment, level of education (high school, apprenticeship, further education college or University) and current employment. A measure of deprivation (multiple deprivation measure (MDM)) was derived from their postcode (219). Data were also collected about family history of cardiovascular disease (CVD), physical activity levels (validated International Physical Activity Questionnaire (IPAQ) questionnaire (220)(221)) and a Mediterranean Diet Score calculated using a validated questionnaire (222). A 2-minute walk test was performed twice, separated by a rest period of at least 30 minutes (223), and the average distance

walked in metres was calculated (224). During the two minutes of testing, participants were encouraged to walk as fast and as far as they could. A Hospital Anxiety and Depression (HADs) questionnaire (225) was used to assess anxiety and depression symptoms, a EQ5D-5L questionnaire (http://www.euroqol.org/eq-5d-products/eq-5d-5l.html) to assess quality of life, a Modified Rankin scale (226) to assess level of disability and a Prochaska stages of change questionnaire relating to physical activity was administered (227). The EQ5D-5L index score was derived from the published UK data-set (228). All participants were offered VO_{2max} exercise testing via either a treadmill or bike and had their follow-up assessment undertaken at 6 weeks post-enrolment when the above measurements were repeated. These assessments were then repeated at the 6 week follow-up review appointment. All assessments, both at baseline and follow-up, were undertaken in the Northern Ireland Clinical Research Facility (NICRF).

The Intervention – '*The Healthy Brain Rehabilitation Manual*'

In terms of programme content, '*The Healthy Brain Rehabilitation Manual*' contained an introduction, telling the user how to use the manual, medical and social information about TIAs/'minor' strokes and how to set goals and action plans for changing certain aspects of their lives. It included sections focusing on topics relevant to cardiovascular risk (smoking, physical and sexual activity, mental health issues (primarily anxiety and depression), community resources (e.g. smoking cessation support; exercise classes), diet and secondary prevention medication). The manual was supported with telephone follow-up by a health professional, a General Practitioner (GP). Participants were given advice about how to know that they were participating in moderate

intensity activity. Those with a pedometer were advised that a cadence of 100 steps/minute corresponds to moderate physical activity and for those who did not have a pedometer, they could use the 'talk/sing test' (229). This was explained to patients at their baseline assessments and was included in the manual as well as being reinforced through the telephone follow-up contacts at 1 and 4 weeks.

Randomisation and blinding

Computer generated randomisation was carried out prior to recruitment and the allocations were concealed in sealed, opaque envelopes until baseline assessments were completed. NH, who was not blinded to intervention allocation, undertook post-intervention assessments.

Study design

There were 3 study arms: the control group, Group 1, received current standard post-TIA/minor stroke care as per current UK guidelines (39)(112). In addition to standard care, Groups 2 and 3 received the intervention programme ('*The Healthy Brain Rehabilitation Manual*'). Group 3 also received a pedometer or a Fitbit Charge, with each participant choosing which they wanted to use, and being encouraged to keep a daily step-count diary. NH advised Groups 2 and 3 regarding the use of the manual and pedometer/diary at the end of their initial meeting and assessment. Participants in Groups 2 and 3 were informed about the national UK physical activity guidelines as well as how to achieve moderate and vigorous physical activity intensity (230). The

pedometer was used to allow participants to set and monitor goals to increase their physical activity levels.

All participants, including Group 1, were telephoned at 1 and 4 weeks to answer any questions regarding their care or use of the manual and, for Group 3, NH encouraged participants to self-set step count targets after reviewing the previous week's daily step counts (209). Step counts were recorded, as reported by participants at the end of week 1 and diary records were reviewed by NH at the 6-week follow-up. Average step-counts for weeks 1 and 6 were calculated by adding the daily totals and dividing by the number of days/ week worn by the participant. During the initial meeting and telephone contacts NH used motivational interviewing techniques (231) and adopting the '5 As' approach to behaviour change (231), which have all been utilised within different healthcare settings (232), including primary care and the community.

Data treatment and statistical analysis

No formal power calculation was undertaken as this was a feasibility study but 5 patients in each of the 3 treatment groups was considered sufficient to allow assessment of the feasibility of recruitment, conduct of proposed assessments and retention. It was also considered that 15 patients' views could provide useful information regarding our research methods and the acceptability of the intervention programme and its refinement for potential use in a pilot trial. Descriptive statistics were reported for baseline and post-intervention measurements, using Statistical Package for Social Sciences (SPSS, version 23) but the main outcomes were rates of recruitment, retention and completion of measures and the acceptability of the intervention. Participants were encouraged to keep a step diary of their pedometer use

and this was reviewed through the telephone contacts at 1 and 4 weeks and then at follow-up (6 weeks). A daily step count average for each of these 3 time points (1, 4 and 6 weeks) was then calculated for each participant using the pedometer.

Two trained review authors (NH, MAT) independently assessed the manual to identify BCTs included, using Michie's BCT taxonomy (128) of 93 hierarchically clustered techniques and a narrative approach was used to describe the use of BCTs within the rehabilitation programme. They met to discuss the BCTs which they had identified and resolve any discrepancies. A third reviewer (FK) was available to arbitrate in case consensus could not be reached, but was not required.

Qualitative work

All participants were invited to attend a focus group that took place at least two months after their completion of the study and they were encouraged to bring their partner or a family member to the focus group. The primary questions of the topic guide (**Appendix VI**) related to research participation and the acceptability of the different stages of the research study (233). The focus group discussion was led by NH, audio-recorded with the consent of participants, lasted approximately one hour and was transcribed by NH. Content analysis was undertaken with the practical purpose of eliciting views about the acceptability and usability of the intervention and research methods and how these could be refined. NH, a male GP, and MD, a male health services researcher/health psychologist, read and reread the transcripts and coded the content independently. NH and MD met to discuss the main areas covered within the transcripts. MC, a female professor of GP, acted as a referee as required as well as appraising critically the categories and the degree to which the transcript

extracts and quotations supported the themes. The transcripts were not returned to participants for comment and/or correction and participants were not asked to provide feedback on the qualitative results. NH has basic training in qualitative research methods whilst MD and MC are experienced qualitative researchers. The independent results of the qualitative analysis and data interpretation were discussed with the entire research team, to ensure clear definition of themes and that appropriate supporting evidence was identified for each. The reporting of the qualitative study and findings followed the guidance set out in the Consolidated Criteria for Reporting Qualitative Research (COREQ) checklist (184).

Results

Recruitment, retention and completion of assessment measures

During an 18-week recruitment period (March to July, 2016) 107 patients with confirmed TIA/minor stroke attended the hospital TIA clinic. From the hospital data recorded, we were unable to determine how many of these were eligible for the study but 28 eligible patients (15 male; 13 female) agreed to telephone contact from NH. Of these, 15 (10 male; 5 female; 53.6%) consented to participate. All of these completed the study and attended the 6-week follow up assessment. Participants completed all the outcome measures apart from the maximal exercise tests for VO_{2max} assessment, which was declined by all participants at baseline and follow-up. Four participants in Group 3 chose to use a Fitbit Charge initially as their pedometer; 2 reported positive experiences using this device, particularly in goal setting and competition with other users but 2 others were unable to use it and transferred to use a pedometer, Yamax Digi-Walker CW-701, with which no patients reported any problems.

Baseline characteristics

The participants' mean age was 69 years; 9 were diagnosed with a TIA and 6 a minor stroke (**Table 5a, b and c**). Mean time from event to enrolment was 20.5 days. Only one had attained University level education; most had retired. The majority (10) lived in the 50% least disadvantaged areas of Northern Ireland. Although 7 were ex-smokers, only one participant currently smoked; mean alcohol intake was <14 units/week. Ten participants had a first degree relative with CVD and most participants were married (13/15). Baseline IPAQ scores indicated that 10 were either inactive or minimally active and many (9/15) reported sitting for over 5 hours daily. In their first week, Group 3 participants averaged over 8,000 steps/day. Baseline mean systolic and diastolic blood pressure (SBP and DBP) were <140/90mmHg in all groups. The total HADs score was elevated in all 3 groups, particularly for anxiety symptoms. Most participants within the study were classed as 'overweight' as per their BMI.

Post-intervention assessment

Groups 3's mean daily step counts increased over the 6 weeks of the intervention by 1407, with a concomitant fall in the numbers in the IPAQ categories of 'inactive' and 'minimally active' (**Table 6**). Participants reported good compliance with the pedometer, wearing it on most days, as recorded in the step-count diary. IPAQ data for Group 2 also showed an increase in physical activity and a reduction in hours sitting per day. The two-minute walk distance increased in all groups, with the greatest increase in Group 3. HADs scores, particularly for anxiety, improved in Groups 2 and 3. There was a wide variation in the rest of the measurements and overall they showed only small changes.

Qualitative findings

Seven research participants (3 male; 4 female) and one partner (female) attended the focus group. Their ages ranged from 55 to 82 years. Four participants were from Group 3, 2 from Group 1 and 1 from Group 2. Qualitative findings were analysed in order to determine participants' views of the manual, the study design and changes needed for a pilot study of the effectiveness of a novel home-based programme for rehabilitation for patients with TIA or minor stroke. The analysis, supported by anonymised quotes (coded by age (years) and sex (M/F)), is reported within three themes relating to the content of the data.

1. **Use of the manual**
2. **The study design**
3. **Suggested changes**

1. Use of the manual

All participants had positive views about the manual. Its content provided reassurance and support, particularly in differentiating between symptoms for which they should seek medical help and those that were not of such significance. Some reported how they referred to it after having received varying information about their condition and risk factors from different healthcare professionals.

> *"…there was some days when I was panicking a bit and I got the book out and I was like, no, that symptom is ok, that's normal…." (55 yrs, F)*

> *"I think this (the manual) should be at doctor (GP) surgeries as well because when you go to speak to the doctor you get conflicting advice at times." (55 yrs, F)*

Participants' comments reflected their fear and uncertainty about their future health, attributed to their experience of sudden onset of symptoms for their TIA or minor stroke. Some appeared to be in denial of their diagnosis, based on a rationale that their symptoms had been mild (predominantly affecting vision and speech; one had right-sided weakness) and transient but their comments also reflected a sense of uncertainty. However, the manual was welcomed by all as a reference source for credible information that helped them to understand their diagnosis.

> *"It (the TIA) just frightened me and knocked my confidence… because you get no warning." (72 year old female)*

> *"You know, for just 10 minutes' worth of symptoms, surely nothing serious could have happened?" (79 year old female)*

> *"I thought it was excellent…….. like a bible" (70 yrs, M)*

Family members also used the manual in supporting decision-making about seeking medical help. Some did so effectively but others were less helpful: one participant's comments indicated how her family members wished they could deny the significance of her symptoms.

> *"…I was just going to go to my bed but my daughter phoned and I said to her the symptoms I was having and she took me straight to Accident and Emergency (A&E) department." (79 year old female)*

> *"My daughters didn't want to read it because if you read it, then it's true…" (55 yrs, F)*

Other information in the manual provided reassurance for those who felt guilty about not being able to fulfil their previous work-life commitments, particularly as they had no visible physical manifestations of illness. Information regarding the relevance of healthy lifestyle behaviours in helping to reduce risk of further events was valued and participants reported having continued to access it after the study programme had ended: some reported that they put the manual in a prominent place to remind them to sustain preventive behaviours. Other comments indicated how family members used the manual to encourage maintenance of healthy behaviours. Those who had received positive feedback about progress in reducing their risk factors attributed this to having followed guidance in the manual.

> *"I felt an awful fraud cause I was off work but there was nothing physically wrong with me…nothing to show " (55 yrs, F)*

> *"I lift it every morning, read a wee bit, remind myself why I'm not smoking, why I'm not eating a whole load of pastries and why I'm avoiding salt….I might just read a line but it's the very fact that it's sitting there, reminding me of what to do right….I find that very important…" (70 yrs, M)*

> *"my grand-daughter has read it from page to page and every time she comes up to see me, she's like, 'grandad, have you done that? Are you keeping to that?" (70 yrs, M)*

> *"The fact that my blood pressure is a lot lower is also very encouraging for me to stay with the programme as I feel the things which I have done have definitely helped me…" (79 yrs, F).*

2. The study design

Recruitment and randomisation

None of the participants considered that any change was needed to the process of recruitment or method of being allocated to study groups.

Intervention components – telephone follow-up

The structure and timing of telephone follow-up calls were well received by all participants who considered that they reduced their need to seek other medical advice. Comments revealed how participants valued the opportunity to share concerns with a professional and ask questions. For example, many participants expressed how they had fears for the implications of their diagnosis on future travel plans and being able to obtain travel insurance

> *"……they made me feel that there was someone out there interested in me and who cares for me." (70 yrs, M)*

> *"...it put your mind at rest because you were thinking, NH is phoning me soon, so I don't need to go to see the GP. I enjoyed the explanations." (55 yrs, F)*

> *"…..are we going to get to go on holiday and will I be able to fly?" (58 yrs, F)*

Intervention components - pedometers

All Group 3 participants enjoyed using their pedometers, setting step-count targets and competing with others regarding their achievement of these. One participant reported

her appreciation of the Fitbit with its provision of weekly email feedback on her performance. However, two participants discontinued using the Fitbit despite research team support, one because of battery problems and one lacked confidence in its accuracy: both used the Yamax pedometer without difficulty.

> *"…it's a competition between me and the wife who walks the furthest" (70 yrs, M)*

> *" It was just so addictive …. I had that visual target to aim for…It would also send me an email at the end of the week, telling me how much activity I had done and I just thought it was brilliant." (55 yrs, F)*

> *"…and the pedometer would always be less (in step-count measurement compared to Fitbit)…." (58 year old, F)*

Outcome assessments

All participants were also content with the number and duration of assessments and with all outcome measures except treadmill exercise testing. They were apprehensive that they would be unable to complete it, given their recent diagnosis. However, 4 participants expressed a readiness to consider undertaking it at the time of the focus group, approximately 2 months after having completed the rehabilitation programme.

> *"I doubt that I would have been able to do the treadmill exercise test within 4 weeks of having the TIA…." (70 yrs, M)*

> *"I would be interested in doing it now…" (58 yrs, F and 79 yrs, F)*

3. Suggested changes

The only changes suggested by study participants related to the manual. One suggestion was to move the explanations about TIA and minor stroke to the beginning of the manual and another was to include a patient's story.

> *"…. the explanation for the TIA (and minor stroke) is at the back of the manual. I think it should be at the start?'" (58 yrs, F)*

> *"people are interesting and it's good to hear their experiences…" (79 yrs, F)*

BCTs used within the manual

Overall, 36 individual BCTs, from 14 different BCT groups were utilised. Examples of how the BCTs were used in each section of the manual are included in **Supplementary Files 1 to 8**. Within Section 1 (Smoking) 16 individual BCTs were used and in section 2, dealing with physical/sexual activity, 11 being used. The commonest BCTs used were "1.1 Goal setting (behaviour)", "3.1 Social Support (unspecified)" and "3.3 Social support (emotional)" – all being used within 5 of the 8 manual sections. The commonest groups of BCTs used within the manual were "1 (Goals and Planning)", being detected 18 times and Social Support (12 times). Two groups of BCTs were not used within the manual, "14 (Scheduled consequences)" and "16 (Covert learning)".

Discussion

These findings indicate that the evaluation of a novel home-based rehabilitation programme, '*The Healthy Brain Rehabilitation Manual*', implemented within 4 weeks

of a first TIA or 'minor' stroke is feasible. There was 100% retention of participants and more than 50% of patients who were invited by the researcher agreed to participate, although it is uncertain that all eligible patients consented to allow contact by the researcher. All but one of the proposed assessments, the VO_{2max} testing, were fully completed at baseline and follow-up. This study also illustrates the acceptability of pedometers as an appropriate method of promoting physical activity to generally inactive TIA and minor stroke patients. The rehabilitation programme was centred on the use of 'goals and planning' and social support as BCTs as well as the manual being a credible source of information to promote behaviour change. A Logic Model has been developed for this feasibility study and is included in **Figure 11** (234)(235).

Comparison with previous literature

In comparison with previous studies of community-based cardiac rehabilitation for patients with TIA or 'mild' stroke, this study has achieved higher rates of recruitment (50% of those invited) and retention (100%). A feasibility study (126) reported 62% retention of 85 patients enrolled and, in a pilot study (103), approximately 50% of 100 invited patients consented to participate and roughly 80% completed the study. Of note, home-based cardiac rehabilitation programmes are reported to improve programme adherence (121) and to show longer-term sustainability of health benefits compared with hospital-based programmes (123).

An interesting finding was that all participants declined to undertake a maximal VO_{2max} test, both pre- and post-intervention, whereas all other assessments were well received. To my knowledge, this is the first study to report this finding. Exercise testing is safe to undertake among patients with TIA and stroke (236) as well as

generally within the elderly population (237) but the current study participants felt unable to complete it. Thus, for further work, the maximal exercise test has been omitted, in its place adding the Timed Up and Go test (238) and accelerometer assessments of physical activity pre- and post-intervention, which are reliable objective measures of physical activity in stroke survivors (239) and amongst the elderly population (240).

The Group 3 participants increased their physical activity by 1,400 steps/day over the study period of 6 weeks. Indeed, walking ability has been demonstrated to be strongly associated with cardiorespiratory fitness (241) as well as being helpful in guiding prognosis in patients with cardiovascular disease (242). Moreover, an increase in steps/day walked after cardiac rehabilitation has been shown to reduce overall risk of mortality and hospitalization (242). Therefore the improvement in physical activity levels (steps/day) demonstrated within this feasibility study could contribute to making our TIA and 'minor' stroke patients live longer as well as healthier lives. Previous studies have also shown that there is potential for larger increases to be achieved with pedometer interventions (88)(94)(95)(243), with potential to reduce cardiovascular risk factors further, particularly amongst those who are the least active. It has been suggested that healthcare workers should enquire regularly about the walking status of their patients and that this should be viewed as another 'vital sign' in healthcare (244). Pedometers are also accurate and reliable in measuring ambulatory activity (46)(87)(88)(89) whilst also being relatively inexpensive. Yamax pedometers have been shown to be the most accurate waist-borne instrument (87)(88).

The intervention appeared to improve quality of life as measured by the EQ-5D-5L VAS scale and mental health, as measured by the HADs questionnaire (225), although

numbers were small and no significance testing was carried out. In keeping with previous work (190) that found a prevalence within TIA survivors of anxiety symptoms of up to 30% and depression symptoms of up to 21%, the focus group participants were anxious and fearful about having future events. Patients appreciated the explanations and reassurance provided by the manual.

'*The Healthy Brain Rehabilitation Manual*' includes goal-setting for behaviour change, with agreed action plans and relapse prevention ('if-then') plans for each behavioural cardiovascular risk factor. These goals and plans are reviewed and refined in follow-up contacts with the health professional/facilitator. The manual includes feedback and monitoring as a BCT, for example, based on review of pedometer step counts. Social support is promoted through contact with health professionals and encouraging the person to share the manual with their family and friends and to get them to join in the behaviour change.

Strengths and Limitations

This is a feasibility study and therefore no statistical analysis was undertaken on the outcomes. Baseline assessments were completed before participants were allocated to different groups, to avoid allocation bias. The qualitative work undertaken included participants from each treatment group, of varying age and both sexes, with a range of different symptoms and experiences and they identified valued components of the rehabilitation programme. The educational attainment of participants was less than third level (post secondary school education), with only one having a University degree and no one reported any difficulty in following guidance or understanding information within the manual. This was reassuring since, in developing it, a

readability check (http://www.webpagefx.com/tools/read-able/check.php), showed it to be readily understandable to 13 to 14 year olds.

The pragmatic approach, whereby TIA and 'minor' stroke diagnosis was made by the lead clinician at each clinic, may have led to variation in the case mix due to differing interpretation of clinical data but this was accepted as a reflection of 'real-world' practice. There was no post-intervention blinding of assessments so that it is possible that some measurement bias may have occurred. Also, Group 3 participants were not blinded to their step counts in the first week of the study, so that the baseline measure may be inflated and not a true reflection of levels of physical activity at this time in TIA and minor stroke patients.

Whilst initial discussions with clinical staff regarding the process of identification and invitation of eligible patients had included a plan to record anonymously the numbers of all eligible patients, this information was not recorded. Thus, although data suggested that 79 of the 107 clinic attendees during the recruitment period were ineligible, this could not be confirmed and limits our interpretation of the feasibility and acceptability of the research.

A strength of this study is the careful approach that has been taken to identifying the 'active ingredients' of the intervention (BCTs). However, this focused on the manual content whilst other BCTs were also involved in the delivery of the programme, during telephone contacts. No monitoring of the fidelity of these contacts was undertaken but this could be achieved in further study.

Implications for future work

To allow further development and evaluation of the intervention, '*The Healthy Brain Rehabilitation Manual*', a pilot study was planned (Chapter 6). This involved:

- More hospital clinics, increasing from recruiting in 1 hospital to 4.
- Ensuring appropriate information was recorded at the recruiting hospitals regarding all eligible patients to allow completion of a study recruitment log.
- Setting step-count goals for physical activity, only Yamax Digi-Walker CW-701 pedometers were used and given to all intervention group participants, with the Fitbits no longer used.
- The maximal VO_{2max} exercise test was discarded and replaced by the Timed Up and Go test (238) pre- and post-intervention, with accelerometer assessments, providing reliable objective measures of physical activity in stroke survivors (239) and older people (240).
- A 'patient story' being included in '*The Healthy Brain Rehabilitation Manual*', in-keeping with previous authors' work (245).

Conclusion

These findings showed the feasibility, acceptability and potential significance of implementing a novel home-based rehabilitation programme, '*The Healthy Brain Rehabilitation Manual*', with or without an added pedometer, in patients diagnosed with a first TIA and/or minor stroke. The main BCTs used within the manual included use of a credible source, social support and goal setting, in keeping with current UK national guidance for behaviour change. This preliminary work then informed the design of the pilot study (Chapter 6), with longer follow-up, recruitment from a range of settings and refined methodology (clinicaltrials.gov (NCT02712385)). This work

should then provide evidence of the value of an early secondary cardiovascular prevention intervention that focuses on behaviour change for patients following TIAs or minor strokes.

Chapter 6

Stroke Prevention Rehabilitation Intervention Trial of Exercise (SPRITE) - A Pilot Study

Introduction

Previous chapters documented (i) the service user input to '*The Healthy Brain Rehabilitation Manual*' (Chapters 4 and 5), (ii) systematic reviews of the underlying evidence (Chapters 2 and 3 with a literature review in Chapter 1) and then (iii) a feasibility study (Chapter 5) – the results of these investigative activities were used to develop the intervention to this point. This chapter explains the next step in the development of the intervention, the pilot study. The pilot study differed from the feasibility study by recruiting from 4 instead of 1 hospital (only the Western Trust in NI did not recruit), compared GP telephone follow-up to stroke nurse telephone follow-up as well as having longer follow-up (increasing to 12 weeks from 6 weeks), tested new outcome measures and the new intervention, which included pedometers, developed from the feasibility study comments. Information from this pilot study will be used to refine the intervention further if necessary and to plan for the next stage in terms of the evaluation of this complex intervention, a full randomised controlled trial.

Reporting a Pilot Study - CONSORT extension for pilot studies (246)

The National Institute of Health Research (NIHR) defines a pilot study as (see 'Pilot studies' entries at http://www.nets.nihr.ac.uk/glossary):

> "……a smaller version of the main study used to test whether the components of the main study can all work together. It is focused on the processes of the main study, for example to ensure that recruitment, randomisation, treatment, and follow-up assessments all run smoothly. It resembles the main study in many respects, including an assessment of the

> primary outcome. In some cases, this will be the first phase of the substantive study and data from the pilot phase may contribute to the final analysis; this can be referred to as an internal pilot. Or, at the end of the pilot study, the data may be analysed and set aside, a so-called external pilot."

Reflecting this definition of a pilot study, Lancaster (247), supported by a recent editorial (248), advise 7 key areas to report in a pilot study to allow judgment on its success:

1) to test out the study protocol and ensure all study components work well together;
2) to perform a sample size calculation for the future randomised controlled trial. That is, the pilot provides an estimated effect size;
3) test out data collection, including outcome assessments and blinding;
4) test randomisation;
5) help estimate rates of recruitment, those consenting and retention. This includes the processes of recruitment, identification of study population, selection of participants, process of consent and of arranging baseline assessment;
6) determine the acceptability of the intervention, including study duration, assessment of compliance and fidelity of delivery and cost/measures captured to allow cost analysis;
7) select the most appropriate primary outcome measure for the future randomised controlled trial.

These 7 areas are very similar to the 14 outcome measures for reviewing pilot studies reported by other authors (249)(250) as well as the CONSORT extension for pilot

studies (246) and I have therefore reported my findings from this study based on the CONSORT guidelines (246).

Aim

The aim of this study was to pilot an adapted home-based cardiac rehabilitation programme, '*The Healthy Brain Rehabilitation Manual*', with an added pedometer intervention and telephone follow-up from either a GP or stroke nurse, in the acute period (within 4 weeks) following a first TIA or 'minor' stroke of atherosclerotic origin and from 4 recruitment sites. The aim was also to obtain an initial estimate of the effectiveness of the intervention in improving cardiovascular risk factors in the TIA and 'minor' stroke population.

Objective

To: (1) determine if it is feasible to pilot '*The Healthy Brain Rehabilitation Manual*', with a pedometer intervention and telephone follow-up from either a GP or stroke nurse, within 4 weeks of a patient suffering a first TIA or 'minor' stroke with 12 weeks of follow-up and from 4 recruitment sites;

(2) assess the patient acceptability of the intervention;

(3) assess rates of recruitment, completion of outcome measures and follow-up;

(4) explore participants' views of the intervention and research methods; and

(5) obtain a first estimate about the potential effectiveness of the intervention in terms of improving cardiovascular risk factors.

The a priori criteria for success within this pilot study were that 30% of eligible patients agreed to the initial study contact, with more than 50% retention of recruited patients.

Methods

Trial registration and Ethics Approval

The study was approved by the Office for Research Ethics Committees, Northern Ireland (REC reference 15/NI/0001, 21/09/2015) and registered (ClinicalTrials.gov, NCT02712385) and I have followed CONSORT guidelines for reporting randomised pilot trials (211)(251) as well as the PREPARE trial guide (213).

Study Setting and participants

Patients attending 4 TIA/ 'minor' stroke assessment units in Northern Ireland (one each at the Royal Victoria Hospital, Belfast; the Ulster hospital, Belfast; Antrim Area hospital, Antrim; Craigavon Area hospital, Craigavon) were given information about the study by the clinical stroke nurse at their hospital assessment visit and asked for their consent to be telephoned by the lead researcher (NH) the following day to invite their participation. Those who agreed attended the Northern Ireland Clinical Research Facility (NICRF), Belfast City Hospital, for an initial meeting where, with consent, baseline data were collected.

Pilot study amendments

On the 11/10/2017, a minor amendment was accepted to allow home assessments for the baseline and follow-up measurements in addition to the option of having the assessments at the NICRF. This amendment was submitted in recognition that participants were travelling across NI to participate in the study, with some return car journeys being up to 4 hours in duration, depending on where the participant resided.

Eligibility Criteria

Eligibility criteria for the pilot were the same as for the feasibility study. To recap, patients were eligible for inclusion if they were aged 18 years or older and within 4 weeks of their first symptoms of a TIA or 'mild' stroke. The diagnosis was made by the consultant at the clinic, based on history, neurological examination and neuroimaging (17). Using the TOAST classification system (214)(215) only TIAs and 'minor' strokes attributed to atherosclerosis or small vessel occlusion were included. Patients who had unstable cardiac conditions or contraindications for exercise training (216), were unable to give informed consent or had a previous cerebrovascular event were excluded.

In each hospital, the clinical and research stroke nurses completed the on-site recruitment log. The recruitment log was either kept on the ward and/or at the clinic. This recorded: the number of patients attending the clinics diagnosed with a TIA and/or 'minor' stroke; those eligible for the study; the numbers of patients accepting the invitation to be contacted by the researcher; and the numbers then entering the study.

Once the patient gave their initial consent, the clinical and/or research stroke nurses emailed the lead researcher with the contact details to enable him to telephone the patient the following day to invite them into the study. The Ulster, Royal, Craigavon and Antrim hospitals all operate daily 'drop-in' TIA clinics whilst also operating set scheduled outpatient clinic times for patients to be assessed. Patients could also be recruited if they were admitted to the hospital directly from, for example, the Accident and Emergency department.

I visited the recruiting centres either once a week or fortnightly to review recruitment processes and records, maintain enthusiasm amongst the staff for recruitment and answer any questions which the staff might have as well as maintaining visibility of the study. All hospitals had a stroke research nurse who was able to support the clinical stroke nurses in the recruitment process. However the research nurse in the Ulster was only in post for a few weeks during the research period. The research nurses in the Royal Victoria hospital were also involved in a number of other research projects and their available time to have input into my study was therefore limited.

Data collection

At the initial and 12 week follow-up meeting, lasting approximately one hour, the researcher and research nurse who was blinded to patients' treatment allocations, measured the same variables as were recorded for the feasibility study (see Data Collection, Chapter 5), except the maximal VO_{2max} treadmill test which was removed following patient feedback after the feasibility study (Chapter 5). The EQ5D-5L index score was derived from the published UK data-set (228). All participants additionally underwent a Timed Up and Go test (238) and were invited to wear a single wrist-worn,

tri-axial accelerometer, Axivity AX3, for one week on their dominant wrist as per the UK Biobank study (252), as an objective measure of physical activity levels. The accelerometer was set-up to start recording from midnight on the first day it was put on by the lead researcher until up to 7 days later. Participants were encouraged to wear the device for 24 hours a day, only removing it for water-based activities, e.g. showering. It was set-up to capture triaxial accelerations at 100Hz and participants were given a stamped addressed envelope to post the accelerometer back to the research centre at the end of the wear period.

The Intervention – '*The Healthy Brain Rehabilitation Manual*'

The content of the intervention, '*The Healthy Brain Rehabilitation Manual*', and the specific BCTs used within the manual have been described in Chapter 5. A copy of the manual that was used in the pilot study is included within **Appendix VII**. The manual was supported with telephone follow-up at 1, 4 and 9 weeks, by a health professional, either a General Practitioner (GP), who was the lead researcher (NH) on the project, or a stroke nurse. Two stroke nurses (Band 6) completed all the telephone follow-up for this study. Participants were given advice regarding how to know that they were participating in moderate intensity activity: if the participants were using their pedometer, they were advised that a cadence of 100 steps/minute corresponds to moderate physical activity; an alternative is the 'talk/sing test' (229). This was explained to patients at their baseline assessments and was included in the manual as well as being reinforced through the telephone follow-up.

Randomisation and blinding

For the randomisation, an independent medical statistician generated random permuted blocks of 3, using numbers from 1 to 3 and placed these in sealed, opaque envelopes, which were opened by the lead researcher after the baseline assessments were completed and before the study was started. A research nurse, who was blinded to intervention allocation, undertook post-intervention assessments. The accelerometry data were analysed by an independent research scientist. Study results were analysed by a medical statistician independent to the research study and who was blinded to participant study allocation.

Study design

There were 3 study arms: the control group, Group 1, received current standard post-TIA/minor stroke care as per current UK guidelines (39)(112)(181). In addition to standard care, Groups 2 and 3 received the intervention programme ('*The Healthy Brain Rehabilitation Manual*') and a pedometer, Yamax Digi-Walker CW-701, whilst being encouraged to keep a daily step-count and physical activity diary. NH advised Groups 2 and 3 regarding the use of the manual and pedometer/diary at the end of their initial meeting and assessment. Participants in Groups 2 and 3 were informed about the national UK physical activity guidelines as well as information on how to achieve moderate and vigorous physical activity intensity (230) and to reduce sedentary time. The pedometer was used to allow participants to set and monitor goals to increase their physical activity levels. These goals were discussed and set during the telephone follow-up.

All participants, including Group 1, were telephoned at 1, 4 and 9 weeks to answer any questions regarding their care or use of the manual and, for Groups 2 and 3, the GP/stroke nurse encouraged participants to self-set step count targets after reviewing the previous week's daily step counts (209). Step counts were recorded, as reported by participants at the end of weeks 1, 4 and 9 and diary records were reviewed by NH at the 12-week follow-up. Average step-counts for weeks 1, 4, 9 and 12 were calculated by adding the daily totals and dividing by the number of days/week worn by the participant. During the initial meeting and telephone contacts by the GP (NH) or stroke nurse, motivational interviewing techniques (231) were used and the '5 As' approach was adopted to promote behaviour change (231). These techniques have been utilised previously within different healthcare settings (232), including primary care and the community. A standard approach to the telephone follow-up was adopted by the GP and stroke nurses, who received face-to-face training with the lead researcher, NH, on how to conduct this follow-up as well as standardised forms being completed (**Appendix VIII**).

Data treatment and statistical analysis

No formal power calculation was undertaken as this was a pilot study but 40 patients in the whole study, spread evenly across each of the 3 treatment groups, were considered sufficient to allow assessment of recruitment, conduct of proposed assessments and retention. It was also considered that a sample of these 40 patients' views and of the recruiting stroke nurses' views could provide useful information regarding our research methods and the acceptability of the intervention programme and its refinement for potential use in a full randomised controlled trial. Descriptive

statistics were reported for baseline and post-intervention measurements, using Statistical Package for Social Sciences (SPSS, version 23) but the main outcomes were rates of recruitment, retention and completion of measures and the acceptability of the intervention. The statistician was independent to the research team and was blinded to group allocation. No statistical tests were performed on the baseline data as per previous authors (253); ANCOVA was performed to compare baseline and post-intervention mean results across the 3 groups (254).

It has been shown that 72 hours of accelerometer wear time is required to be within 10% of the 7 day value (252) and I therefore analysed all output with data for more than 72 hours. The accelerometer data was compared to the individual's physical activity diary and non-wear time was defined as consecutive stationary periods lasting 60 minutes or longer as per previous authors (252), with all non-wear time being removed prior to analysis. The output data was split up into sedentary time and then light, moderate and vigorous physical activity, with an average taken for each of these variables during the true wear period. The moderate and vigorous physical activity averages were added together to allow the moderate-vigorous physical activity (MVPA) values to be calculated.

Blinding

Blinding of participants, the GP and stroke nurses was not possible due to the nature of the study intervention. However an independent nurse carried out all the 12-week follow-up assessments, ensuring blinding of the study group allocation for the follow-up assessments. The study statistician and the research assistant for the accelerometer analysis were both blinded to study group allocation when carrying out their analysis.

Qualitative study

Seven participants were invited to attend a focus group, selected purposively to include a range of different genders, ages, clinical conditions and research group allocations. Four of these seven then attended the focus group, which took place at the completion of the study. There was also an end of study focus group undertaken with the 2 stroke research nurses who delivered the follow-up contacts within the intervention for Group 3 within the study. The primary questions of the topic guide (**Appendix IX**) related to research participation and the acceptability of the different stages of the research study (233). The focus group interviews were led by NH, audio-recorded with the consent of participants, lasted approximately one hour and 20 minutes, respectively, and were transcribed by NH. Content analysis was undertaken with the practical purpose of eliciting views about the acceptability and usability of the intervention and research methods and how these could be refined. NH, a male GP, and MD, a male health services researcher/health psychologist, read and reread the transcripts and coded the content independently. NH and MD met to discuss the main areas covered within the transcripts. MC, a female professor of GP, acted as a referee as required as well as appraising critically the categories and the degree to which the transcript extracts and quotations supported the themes. The transcripts were not returned to participants for comment and/or correction and participants were not asked to provide feedback on the qualitative results. NH has basic training in qualitative research methods whilst MD and MC are experienced qualitative researchers. The independent results of the qualitative analysis and data interpretation were discussed with the entire research team, to ensure clear definition of themes and that appropriate supporting evidence was identified for each. The reporting of the qualitative study and

findings followed the guidance set out in the Consolidated Criteria for Reporting Qualitative Research (COREQ) checklist (184).

Patient and Public Involvement (PPI) Group

The PPI group included 2 participants, one female who volunteered to be part of this group following the feasibility study, and a gentleman who had suffered a stroke and who was a member of the local Stroke Association. Part of their remit was that they were asked to grade the outcome measures, from 1 (perceived as being most important) to 15. This was done by giving the participants a list of all the outcome measures on a piece of paper and they then wrote beside each outcome measure the score/number they had given it. I also met with them on a regular basis and discussed the study's progress and encouraged their regular critique of the study methods and findings.

'Stop criteria' for the pilot study

Criteria for stopping the pilot study prematurely were developed as per recent guidelines (255) and included:

- Failing to achieve the a priori criteria of recruiting 30% of eligible patients to the study;
- Failing to retain more than 50% of recruited patients to the study;
- More than one cardio- or cerebrovascular event, for example a further stroke event or myocardial infarction, in the treatment arms of the study (Groups 2 and 3);

- Recruiting centres being unable to recruit eligible patients;
- Recruiting centres not completing the on-site recruitment log; and,
- Protocol non-adherence, including for the research measurements and the actual study intervention.

Results

Recruitment, retention and completion of assessment measures

During 32 weeks of recruitment (week beginning 08/05/2017 to 22/12/17) 443 patients with confirmed TIA and/or 'minor' stroke attended the 4 recruiting hospitals (see **Figure 12** for CONSORT study flow diagram). From the hospital data recorded, there were 125 eligible patients (28.2%) and 44 (35.2%) of these agreed to telephone contact from NH (see **Table 8**). Of these, 40 (90.9%) (24 male, 60%; 16 female) consented to participate and all participants were white British and/or Irish citizens. Thus the a prior objective of at least 30% of eligible patients agreeing to the initial study contact was achieved.

From the 4 recruitment centres: 16 were recruited from the Ulster Hospital; 12 from the Royal, Belfast; 8 from Craigavon Area Hospital; and, 4 from Antrim Area Hospital. Three eligible patients from the Royal site were not given an invitation to enter the study in December due to time constraints on clinical staff and this was not identified in time by the research nurse to allow the patients to be given the opportunity to enter the study. These patients have still been included in the recruitment numbers relating to eligible patients. The main reasons for people not being eligible for the study included having previous cerebrovascular events, the event being more than one month ago and the cerebrovascular event being non-

atherosclerotic in origin or not due to small vessel occlusion, as per the inclusion criteria.

There was 1 study drop-out: 1 female subject (randomised to group 3) dropped out after she had completed baseline assessments, including wearing the accelerometer but before beginning the actual intervention due to work commitments. The remaining 39 patients completed the study and attended the 12-week follow up assessment (see **Figure 12**, CONSORT flow diagram). All participants completed all the outcome measures. Twelve patients (8M, 4F) were randomised to Group 1 (control) whilst 14 were each randomised to Groups 2 (GP follow-up) (10 M, 4 F) and 3 (stroke nurse follow-up) (6M, 8F) respectively.

Two patients had home baseline assessments after a non-substantial amendment was accepted on 11/10/2017 and in both cases, primarily due to geographical distance from Belfast and not being able to drive a car one month following their event, they would not have been able to participate in the study if the home assessment was not in place. They were both able to attend the NICRF, Belfast for the follow-up assessment at 12 weeks, ensuring blinded follow-up assessment.

Baseline characteristics

The participants were aged from 38 to 88 years old with an average age of 63 years old in Group 3 to 70 in Group 1; 26 were diagnosed with a TIA and 14 a minor stroke (**Table 9a and b**). Group 1 (control) contained 6 TIAs and minor strokes; Group 2 had 12 TIAs and 2 minor strokes; whilst Group 3 had 8 TIAs and 6 minor strokes and thus, there was a slight preponderance of TIAs in the intervention arms. Mean time from event to enrolment ranged from 15 days in Group 2 to 19 days in Group 1. Only a minority of participants had attained College or University level education with the

majority (27/40, 67.5%) being educated to High school level. In terms of employment, 18 participants remained in active employment following the diagnosis with 3 unemployed and 19 retired. There was essentially an even split between participants living in the 50% least and most disadvantaged areas of Northern Ireland. Although 9 were ex-smokers, only 11 participants currently smoked and just under half (19/40, 47.5%) had never smoked; mean alcohol intake was <14 units/week in all 3 groups. Nineteen participants had a first degree relative with CVD, with 5 (12.5%) participants having no significant contact with health services prior to their TIA/'minor' stroke and most participants were married (25/40).

Baseline IPAQ scores indicated that 21 participants rated themselves as inactive and the majority (29/40, 72.5%) reported sitting for 5 hours or more daily. The objective accelerometry sedentary data was similar in all 3 groups at baseline, being approximately 20.5 hours per day. In their first week, Group 2 and 3 participants averaged 5,546 (SD 4,127) and 6,538 (SD 3,993) steps/day, respectively. Whilst the average moderate-vigorous physical activity (MVPA) durations each day varied from 2 hours in Group 1 to 3 hours in Group 3. Baseline mean systolic and diastolic blood pressure (SBP and DBP) were <140/90mmHg in Groups 2 and 3 with baseline mean SBP being slightly higher at 140.4mmHg in Group 1. Baseline SBP and DBP was lowest in Group 3 and only 14 patients at baseline had their SBP within the treatment target of less than 130mmHg (14). The total HADs score was elevated in all 3 groups, particularly for anxiety symptoms and the highest levels were seen in Group 3. Most participants within the study were classed as 'overweight', with the highest average waist circumference (104cm) seen in Group 1. The average 2MWT performance varied from 128 metres in Group 1 to 144 metres in Group 2, whilst the average TUGT varied from 10.5 seconds in Group 3 to 13.3 seconds in Group 1. Compliance

with the Mediterranean diet was poor across all 3 groups, with the mean score varying between 3 and 4.

Post-intervention results

The follow-up results are included within **Table 10a, 10b, 11a and 11b**. In terms of the cardiovascular risk factors, smoking status improved in all 3 groups. Average SBP reduced in Group 2 (from 137.9, SD 16.36 to 127.6, SD 9.95) whilst remaining stable in Groups 1 and 3. DBP and mean resting heart rate essentially remained unchanged in all 3 Groups. The improvement in SBP in Group 2 was reflected by an increase in the number of patients being within treatment guidelines for their SBP (14), that is, SBP less than 130mmHg, whilst Group 1 had fewer people within this target at follow-up. The average 2MWT performance deteriorated in Group 1 at follow-up (126.6m, SD 45.84) compared to baseline (127.5m, SD 33.09) whilst it improved in both Groups 2 (from 143.5m, SD 53.76 to 159.0, SD 50.27) and 3 (from 142.2m, SD 38.59 to 160.4, SD 37.79). All 3 groups improved their average TUGT performance although the largest improvement was seen in Group 2 (from 12.9 seconds, SD 7.04 to 9.34 seconds, SD 5.80). There was also a decrease/improvement in the average total HADs and anxiety score of the HADs questionnaire in all 3 groups whilst the total mean depression score of the HADs questionnaire improved in Groups 2 and 3 but deteriorated in Group 1 (from 3.08, SD 1.93 to 3.75, SD 2.70). The biggest reductions for the HADs questionnaire within Groups 2 and 3 were seen in the anxiety scores. The HADS scoring was reflected in the mean EQ5D-5L score, which improved in Groups 2 and 3, with the biggest improvement in Group 3, whilst deteriorating in

Group 1. The average EQ5D-5L VAS score improved in Groups 2 and 3 from baseline but Group 1 essentially remained unchanged.

Mean alcohol intake increased in Group 1 and 3 and remained unchanged in Group 2 at follow-up compared to baseline. However all 3 groups had a mean alcohol intake which was within recommended national UK alcohol limits both at baseline and at follow-up. Average weight increased in Group 1 from baseline and reduced in Groups 2 and 3 with the biggest reduction in Group 2 (from 88.05kg, SD 21.43 to 86.45kg, SD 20.43). This finding was similar for mean body mass index (BMI) and waist circumference. There was no significant change in scores on the modified Rankin scale or in the number of patients reporting appropriate secondary prevention medication at follow-up compared to baseline.

In terms of physical activity measures, all 3 groups increased their mean IPAQ scores (MET.minutes/week), with the biggest increase in Group 3 and smallest in Group 1. This corresponded with more people being categorised as highly physically active (HEPA) at follow-up in all 3 groups. Again all 3 groups reduced the amount of self-reported time sitting from baseline to follow-up but the biggest reduction was in Group 2 and there was a reduction in the number of people sitting for 5 or more hours per day at post-intervention in Groups 2 and 3. The number of steps/day achieved in both Groups 2 and 3 increased at follow-up although the biggest increase was in Group 3 (6,710, SD 4585 versus 8,423, SD 4,686 steps/day, respectively). Groups 2 and 3 also reported an increased intention to engage in physical activity. Group 3 had the lowest number of total health contacts (31 compared to the highest of 38 in Group 1) although Group 2 had the lowest mean number of health contacts (2.07, SD 1.39) due to the study drop-out. The between group differences in health contacts were, however, generally small.

In relation to use of the pedometer, 18 out of the 28 (64.3%) participants given a pedometer reported a good user experience and continued to use it throughout the research study. Three participants, all aged over 80 years (2 females and 1 male, 2 from Group 2 and 1 from Group 3) and who were generally frail, felt that the pedometer was under-counting their daily steps but they continued to use it and their data were included in the results reported although on reviewing these participants' step and physical activity diaries, the pedometer did appear to be under-counting. One participant was unable to use the pedometer as they were in a wheelchair, whilst 5 (17.9%) participants lost their pedometer. A further female participant stopped using the pedometer as she felt it was irritating her waist when she wore it.

One of the participants, randomised to Group 3, was permanently in a wheelchair and their 2MWT, TUGT, height and weight could not be measured.

Further stroke events and adverse events

There was one further stroke event during the follow-up period that occurred in a female participant in the control group. There were no other adverse events reported during the follow-up period.

Accelerometer Data

Forty patients completed the baseline accelerometer assessment, wearing the device on their dominant wrist for 9 consecutive days. Thirty nine patients completed the post-intervention accelerometer assessment: one patient completed her baseline accelerometer assessment but did not start the actual study intervention. Two post-

intervention accelerometers were lost in the post as both participants reported returning it in the pre-paid envelope but it was not delivered to the research office. The accelerometer data were compared to the physical activity and step-count diary records, which each participant was asked to keep, to encourage physical activity and ensure accelerometer fidelity. Accelerometer data were only used for people with at least 72 hours' worth of monitoring. The baseline data of one participant, randomised to Group 3, were excluded as they only had 48 hours of data. The accelerometer data was analysed by day and non-wear time was excluded. For the analysis, I used the Esliger formula within the Axivity software for either the left or right wrist, depending on the person's dominant hand (and therefore the hand on which they wore it). Although there was no statistically significant difference in accelerometer data between the control group and either intervention groups, there was an overall trend for Group 2 to increase their objectively measured physical activity from baseline and to reduce their average daily sedentary time. Indeed Group 2 increased their baseline MVPA from 163.6, SD 68.75 minutes/day to 190.2, SD 103.9 minutes/day at follow-up and the biggest increase was seen in the amount of moderate physical activity being undertaken. The sedentary and MVPA times in Groups 1 and 3 remained unchanged from baseline.

PPI Group

The PPI group ranked the outcome measures used within the feasibility and pilot studies based on their perception of their importance. Systolic blood pressure was consistently ranked as the number 1 outcome measure.

Qualitative findings

Four research participants (1 male; 3 female) and 2 stroke research nurses (2 female) attended the focus groups. Their ages ranged from 50 to 83 years. Three study participants were from Group 3 and 1 from Group 2. Qualitative findings were analysed in order to determine participants' views of the manual, the study design and changes needed for a randomised controlled trial of the effectiveness of a novel home-based rehabilitation programme for patients diagnosed with either a TIA or minor stroke. The analysis, supported by anonymised quotes (coded by age (years) and sex (M/F) whilst N1 and N2 was used for the nurses), is reported within four themes relating to the content of the data.

1) **Use of the manual;**
2) **Study design**
3) **TIA or 'minor' stroke sequelae**
4) **Suggested changes to the study/manual for future work**

1) Use of the manual

The manual was generally well received and overall the stroke research nurses reported positive patient feedback about the manual, particularly the physical dimensions of the manual:

> *"So the size was nice, it was nice to handle and it was very clearly written. There was good feedback from patients in general about the manual." (N1)*

Participants read the manual in different ways. One participant in the focus group read the manual once to get the main health messages:

"I just read it as a one off and got the gist of it and that was good enough for me but it might not be good enough. I read it and then just got an idea about diet and exercise, so the message was there." (60yo, male).

Another focus group participant supported this although the telephone contacts also caused her to re-read the manual:

"yes, I read the manual like you said and then when the nurses rang, I was like, oh I better get the manual out again and read over those sections again…" (83yo, female)

Other participants enjoyed reading small segments of the manual and then discussing the information with the health professional through the telephone follow-up. Whilst the diet section and physical activity diary of the manual were particularly well received by participants. Other participants reported that their family read the manual and this helped them to adopt the healthy living advice contained within the manual:

"it works well when you read it and then discuss it with someone. I thought the follow-up telephone calls were very good and you could discuss what was in the manual with the stroke nurse on the phone. She could then point out things which might be useful and things to pick up on…" (57yo, female)

"I think it did encourage me to eat better and so I now, for example, try to eat more green vegetables, eat more fruit and generally try to eat a better breakfast, porridge in the morning for example. So it has influenced my diet." (83yo, female)

"I think the activity diary is a good idea." (57yo, female)

"yes my daughter too (read the manual)….. well my daughter was taking in the information in the manual very closely and then she was getting me to, you know, better diet and all the rest of it. …So she tried to help me with easy to make healthy food, that's good for you. So she took an interest in the manual." (60yo, male)

Participants enjoyed having diagrams to support the information contained within the text of the manual and this encouraged them to adopt the appropriate behaviour change:

"the easiest thing for me was, with regards eating, was the picture of the plate with the proportions you should have on it. So for example, half your plate should be vegetables." (60yo, male)

2) Study design

a. Recruitment and randomisation

Participants did not have any issues with the recruitment process and were keen to participate in the research project as they felt it provided them with some follow-up following the TIA or 'minor' stroke, which is not currently available within routine care in the National Health Service (NHS).

"I thought that was a good thing. It was good to have some aftercare so to speak." (60yo, male).

"I was exactly the same. I was really glad that there was something there as a back up because I wasn't sure myself about the medication. At the start I

wasn't sure if I was taking it at the right time or whatever, so I was really glad that there was something there." (78yo, female)

"….yes I was the same. I was quite pleased to have some follow-up as I got quite a shock after my stroke, as I didn't realise what I had. It was quite a mild one but nevertheless, I was glad to have someone follow me up and to know if there is something I can do to avoid having another one…" (83yo, female)

This was supported by the stroke research nurses who were assisting with study recruitment and who also reported that putting information about the research groups onto 3 pieces of paper, a 'study plan' as they called it, in addition to the study paperwork provided, aided recruitment:

"One of the things we did was made up a study plan and gave people the 3 options so they could easily and more quickly see the 3 study options. Once you explained the study to participants, people were really interested but most were very keen to get into the intervention arm." (N2)

Participants did not have any issues with attending the Northern Ireland Clinical Research Facility (NICRF), based in Belfast, despite the fact that it was often quite a distance from their home or their recruiting hospital although travel expenses were covered for study participants:

"I thought it was easy (to get to the NICRF)." (57yo, female)

Again the stroke research nurses supported the patients' views on this although they recognised that perhaps the travel distance and the logistics of actually getting to the NICRF potentially discouraged more elderly, frail patients:

> *"maybe it put a couple of people off if they knew they had to travel that distance. But I don't think it was a major factor….it maybe put off some of the more elderly participants, who perhaps didn't have any form of transport." (N1)*

Some study participants commented on the logistical challenges of attending the NICRF, which is based on a ward of one the local hospitals in Belfast, for example car parking:

> *"this time I took a taxi but I'm not sure if you remember the last time I left here, it was bucketing (raining), I had to push my rollator up to the top of the car park…..Anyway I had to walk up there to the car park and by the time I got home, I was drenched. So today I thought, I'll take a taxi. I live outside xxxx, so it was handy…." (83yo, female)*

The patient focus group discussed an alternative recruitment method involving holding a recruiting clinic for the research study at the same time as the hospital clinic or in their local hospital a few days later. Although people recognized the potential benefits of this approach, they did not feel that it was better than attending the NICRF for recruitment to the study.

In terms of increasing access to the research study, the stroke nurses felt that including participants who had previous cerebrovascular events as well as including those who had a TIA and/or 'minor' stroke due to, for example, atrial fibrillation, could widen study eligibility criteria:

"the 2 things which restricted our recruitment was the past medical history of TIAs and strokes and then people who had an event due to cardioembolic causes…" (N2)

"yes….having a previous event, ruled out a lot of people…." (N1)

b. Intervention components

i.Baseline assessment

One participant felt that the baseline meeting with the researcher was an integral component of the intervention, when the goals for the research study were set and the intervention was tailored to their needs. They also reported that they enjoyed the monitoring performed through the use of the pedometer as well as the review telephone calls and appointments to monitor their compliance with the behaviour change:

"I think the actual meeting with you is more powerful than reading the manual. I think if you're saying, look, this is what you need to do – try and do 7500 steps/day, here's a pedometer, I thought that was a really good idea, then it's back to the individual to either do it or not do it. The other thing was you know you're coming back, so you have that accountability, so you're saying, well try and do this amount of exercise and can you come back and here is a pedometer to monitor yourself, I think that was very good…accountability. You know, put the onus back on yourself and knowing what you had to do." (60yo, male)

ii.Telephone follow-up

Participants enjoyed the telephone follow-up and reported no difference between the stroke nurse and GP follow-up. The group also felt that the telephone follow-up helped their compliance with the programme whilst not being too time consuming. Indeed the average length of a telephone call was approximately 5 minutes. The stroke research nurses also reported that it wasn't too time consuming to undertake the telephone follow-up from their perspective, with most participants answering the phone on their first attempt at trying them:

> *"I don't think it makes a difference if you're followed up by a GP or stroke nurse because it's all about the conversation and the questions you were asked." (57yo, female)*

> *"I thought it was motivating…. they would give you a call and it was good that someone was showing an interest in you." (60yo, male)*

> *"….it (the time duration) wasn't significant." (83yo, female)*

> *"most of the people I phoned, I got them first time. There was only a couple of people who I had to phone a couple of times." (N1)*

All focus group participants reported that having the 3 telephone calls over the 12 weeks of follow-up was sufficient and they did not identify any other form of follow-up (e.g. online) as an alternative to this.

The stroke research nurses enjoyed the telephone calls overall and felt confident in performing them but felt that it could be initially challenging phoning a patient as they had little clinical information about them. They suggested that this could be overcome by giving them access to their electronic healthcare record.

"The thing which I found difficult was the fact that we were phoning people up from other trusts, 'cold' if you like, there was no background." (N2)

"I suppose one way round that would be to give us access to their health and care number, so that if something does crop up then you can go in and you have their medical history and medication…." (N2)

iii.Pedometers

The pedometers were generally well received as a monitoring tool for physical activity levels although one participant commented that it was under-counting the number of steps they took:

"….it didn't work for me. Sometimes it said I had done a few hundred steps and other days, thousands. It wasn't recording all my steps which I had done. I'm not sure what it was but it didn't work." (83yo, female)

The stroke research nurses did not generally feel confident about counselling the patients regarding the pedometers and recognised that this could have been overcome with some training:

"I wasn't too good at that (advising participants about the pedometer) because I'm not too good with technology plus I hadn't actually seen the pedometer." (N2)

iv.Outcome assessments

All the participants commented that the baseline and follow-up measurements were appropriate and had no issues with performing any of these.

> *"…..they were fine to do." (57yo, female)*

v.Dissemination

In terms of research dissemination, all the participants wanted to know about the outcomes from the study but key to this was keeping their information anonymous.

> *"if there is anything which would be useful, then I would want to know. For example, what I want to know about is the risk factors for having a stroke and then recommendations about what I should be doing to prevent having another one. So I think information like that in the public can't be anything other than good. As long as we are anonymous." (83yo, female)*

> *"certainly from my point of view, I would be interested to know how it turned out for different kinds of people with different types of stroke and how this compared to people who didn't do the programme, if that is possible." (57yo, female)*

> *"But like I say, if people in our position (who have had a TIA or minor stroke), could be told about the programme, then that would be good." (60yo, male)*

It was also suggested that efforts could be made to target information to those considered to be at high risk of having cerebrovascular events so they could modify

potential risk factors. Although it was recognised that health information can potentially have negative consequences.

> *"…..maybe also tell family members who have a strong family history of strokes and are perhaps predisposed." (57yo, female)*

> *"…..but even with a family history, you don't want to be scaring the life out of people and them thinking they are going to have a stroke just because their relative has had one…" (83yo, female)*

The stroke research nurses felt it was important to let the local and national stroke charities know about the research findings as well as publicising the results through appropriate conferences and the scientific press:

> *"I would let the Stroke Association (UK) and Chest, Heart and Stroke (NI) know about the research findings, so they could publicise this. Also the NI Stroke Forum to present your research at and then publish your findings in appropriate journals. " (N1)*

They also identified displaying the results of the project in clinical areas to let patients know about the findings:

> *"also have something at the TIA clinics about the research project and results, for example a poster or flyer or something." (N2)*

3) TIA or 'minor' stroke sequelae

Participants attributed various symptoms to their event, including hoarseness, and described a sense of shock following the diagnosis as well as reporting a continual worry about having further cerebrovascular events.

> *"sorry I'm a bit hoarse….this hoarseness is definitely a result of the stroke…" (83yo, female)*

> *"yes I got a shock as well when mine was diagnosed…." (78yo, female)*

> *"my fear is taking another one…." (78yo, female)*

Whilst others reported an increase in anxiety following the initial event and fatigue:

> *"The other thing I would mention is anxiety, it's definitely a factor after my stroke. Just worrying about stupid things, things which might never happen." (83yo, female)*

> *"But what I do find, particularly if I try to do as much as I used to, then the next day I'm very tired. Is that part of the stroke?" (83yo, female)*

Expressive language was also an issue for some patients with others identifying effects on memory or cognition:

> *"one thing I found after my stroke, is struggling over words. Even now. I thought it would be better by now." (60yo, female)*

> *"yes, or you get up to do something and you forget why you got up?" (83yo, female)*

These are all persistent symptoms which the patients therefore felt should be addressed within the manual.

4) Suggested changes to the study/manual for future work

The research study was generally well received:

> *"….in general it was very good and I think it was a very positive thing to be involved with, with lots of positive feedback from the patients themselves." (N1)*

However there were some suggested changes for developing the project further.

a. Electronic version of the manual

For the next stage in the development of the manual, participants suggested an electronic version, for example as an app on a phone:

> *"I think it's (an app on the phone) a good idea…" (83yo, female)*

However the stroke research nurses recognised the need to provide both electronic and paper copy versions to allow patients to decide which version they preferred:

> *"I think you would have to give people both options but yes, it's a good idea." (N2)*

b. Cognitive tests

One patient made comment that they felt it would be useful to include an assessment of cognition for the follow-up tests:

> *"you could maybe do some mental tests as well? Just a thought. You could ask for people to do calculations or something and compare them between the beginning and end." (57yo, female)*

c. Accelerometers

The group recognised that the season of the year influenced their activity levels and that using the accelerometer for longer than a week would be more reflective of their activity levels:

> *"it might be better to wear it for longer than a week because, for me anyway, walking in the bad weather just doesn't happen. The good weather then comes along and you're doing 7500 steps or more everyday, no problem. In the bad weather it might just be 2000 steps or so a day….. Maybe even a couple of months would be a better reflection." (60yo, male)*

> *"yes there is a difference between winter and summer." (57yo, female)*

Feedback was important for participants. Indeed one participant commented that they were keen to know the result of the accelerometer and that this should have been discussed with them after the baseline and follow-up assessments.

> *"we never heard how we did with the black watch (accelerometer)." (83yo, female)*

d. Open questions

Despite the baseline and follow-up assessments having offered a number of opportunities to ask questions, one participant made comment about potentially having some more open questions during the assessments to allow more of a conversation to develop. They also wanted the researcher to encourage the participants to write down appropriate questions to ask the health professionals at their next contact.

"….So instead of asking a set number of questions, leave it a bit more open and then ask the person how did they find everything and do they have any questions? You know you asked questions about are you fearful and how are you feeling but there were things which you didn't ask, that when I went away and thought about things, there were a few things that I would have liked to have been asked. So I think if there was more of a conversation, they might have come out, I don't know but they might have. So maybe leave a space for more free speech or whatever…. Perhaps even say, before the next time you come down or see me, write down a few questions in the manual which you would like to ask me." (60yo, male)

e. Food diary

It was suggested by 2 study participants that a food diary be added to the manual:

"I did get into the habit of keeping a food diary and it wasn't too bad to do. It's just unbelievable to see how many sweets I eat. You don't know how bad your diet is until you write it down and then you read it. I mean I wouldn't have thought I would eat more than 3 bars of chocolate a month but then when it is written down, it's more like 10 or 12." (57yo, female)

One way of doing this, is by utilising technology, for example, apps on smartphones and participants felt this would put the emphasis back on the patient to allow them to take ownership of changing different aspects of their unhealthy lifestyle:

"yes I have an app, MyFitnessPal, and it has a food diary, so you tap into it. It recognises foods, so you can scan bar codes and it tells you the calories

and so on. I thought it was really good. It's good again for accountability." (60yo, male)

Some commented on the potential adverse effects of monitoring behaviour too closely:

"you can't let it control your life though! You can begin to get a bit tyrannical." (57yo, female)

f. Longer duration follow-up

The 12 week study duration was well received by the study participants:

"…not too long, not too short. It was enough time to see an improvement." (57yo, female).

The idea of a longer study duration was also well received:

"….it wouldn't be a problem for myself". (60yo, male)

This view was also supported by the stroke research nurses and 6 months was suggested as an appropriate study duration:

"Yes, I think that would be good actually, as 12 weeks is quite short. Yes 6 months would be good and I think people would benefit from it as well." (N1)

The longer study duration was seen as a positive in combating complacency which can occur following the diagnosis of a TIA or 'minor' stroke, particularly as the person gets further from the event, and in ensuring that the positive behaviour changes become habitual.

"….for me, it's hard to keep motivated. In the first few months you are like, as I mentioned, you're out walking, you're careful with your diet. As time goes on and you get the confidence that you're not going to have another one, there is a danger that you can just drift back into bad habits, same old, same old……. yes, bad habits can come back and maybe having the 6 month review might motivate you further to get into a real life change habit." (60yo, male)

Discussion

This is the first pilot study on the use of an adapted home-based cardiac rehabilitation programme, '*The Healthy Brain Rehabilitation Manual'*, for use in those with a TIA and/or 'minor' stroke of ischaemic or atherothrombotic origin. The pilot study a priori hypotheses were achieved: 35.2% of eligible patients who were invited to consent to an initial telephone contact agreed; 90.9% of patients who received an initial telephone contact to explain the study consented to participate, with 97.5% of these completing the full study. All the outcome assessments were completed and positively received by participants. However, there was no pedometer data for 7 of the 39 participants.

The intervention Groups (2 and 3) generally improved their cardiovascular risk factors compared to the control group (Group 1). In terms of objectively measured physical activity, Group 2 increased the amount of MVPA being undertaken as measured by accelerometry at follow-up compared to baseline and reduced their sedentary time, suggesting a potential positive effect of the intervention. As was evident from the focus group findings and the recruitment and retention rates, this intervention was acceptable to and welcomed by patients. These positive findings indicate the need to further develop the intervention, '*The Healthy Brain Rehabilitation Manual*', and to

evaluate its effectiveness in managing cardiovascular risk factors for the TIA and 'minor' stroke population within an appropriately powered randomised controlled trial.

Eligibility, Recruitment and Logistics of a Multi-centre Trial

Recruitment was from 4 centres from across the region and of 125 eligible patients, 44 (35.2%) consented to telephone contact from the main researcher to be invited into the study. Of these 44, 40 (90.9%) agreed to enter the study and all the 40 patients appeared happy to be randomised, including to a control arm, for the 12 week study duration. The process for achieving randomisation worked smoothly.

The sample size of 40 within the study was appropriate for a pilot study. Indeed Cocks (256) has argued that pilot studies should have at least 9% of the main study's sample size whilst other authors (257) advocate having a minimum of 12 patients in each treatment arm, giving a total potential sample size of 36 for my study. There was one drop out from the study and this one subject stopped her participation before actually starting the intervention but she did complete her baseline assessments, including her accelerometer. Thirty nine participants completed the full study and their 12-week follow-up assessment. This study adherence (97.5% of people randomised completed the study) again illustrates the acceptability of the study procedures as well as the study intervention.

Greaves et al (258) carried out a pilot study in UK primary care of a weight reduction intervention in those identified to be at high cardiovascular risk and overweight. They reported that 22% of those approached to enter the study actually agreed to enter the

study and 89% remained in the study, providing data at 12 months of follow-up. Greaves et al (258) reported that these recruitment and retention rates were acceptable and proved that their pilot could be trialled in a full-scale randomised controlled trial. A further study reviewed the use of physical activity prescription in post-TIA patients (259) and had a drop out rate of 30%. The a priori criteria for success in the current pilot study was that 30% of eligible patients would consent initially to participate in the study and that 50% of those entering the study would complete it. From the recruitment (35.2%) and retention rates (97.5%) and the positive feedback from the study participants, this intervention was well received and acceptable.

In terms of recruitment, a research nurse appointed to one hospital to help with recruitment, unfortunately left the post within one month of the study commencing. The majority of the responsibility for recruitment within that hospital then fell to one clinical stroke nurse, who did this in addition to her normal, already busy, clinical duties. Due to clinical staff commitments, another hospital found it difficult to give patients appointments within 4 weeks of their first event, and there was other on-going research making it difficult to get a 'recruitment champion' at this site. Recruitment in the other two hospitals was helped by the presence of research nurses who kept accurate and current recruitment logs. Having dedicated stroke research nurses at each recruitment site would further improve recruitment numbers for a definitive trial. Another suggested improvement to aid recruitment was for the research team rather than the clinical team to recruit directly from the TIA clinics and wards. This suggested approach would take away the need for a further visit for baseline assessment and was approved in post-study qualitative work. However this method of recruitment would need to be agreed by the ethics committee and by the recruiting hospitals allowing use of their premises for recruitment.

A study by Jancey et al (260) described the effective recruitment strategies used by the PALS study, which was a randomised controlled study of a community-based walking programme for adults aged 65-75 years in Australia and who were classed as insufficiently active. They found that females were more likely than males to be recruited, in keeping with previous study findings (261). They also found it harder to recruit less educated people and had an overall drop-out rate of 28%. Recruits to the PALS study deemed feedback important and the intervention was based locally: these factors all helped with study retention. In contrast to the PALS study, the current study recruited more males than females (24 v 16, 60% v 40%), with a large proportion of patients only educated to high school level and from a high level of socio-economic deprivation, which may reflect the gender and socio-economic distribution of those who were eligible for the current study. These are patients who need targeted secondary cardiovascular prevention to help address some of the known health inequalities (262). The high levels of recruitment within these groups may be explained by the intervention being home-based, recognising that home-based interventions promote greater adherence than community- or hospital-based approaches (121), as well as by the use of specific behaviour change techniques which have been shown to promote better intervention adherence (136).

Noah et al (263) performed a meta-analysis of randomised controlled trials reviewing the effect of wearable technology across different health conditions. Although no statistically significant difference was found for the clinical outcomes, they found that interventions based on health behaviour theories and “personalised coaching” were most effective. Indeed the current intervention includes feedback, monitoring, goals and planning being provided to participants via health professionals through telephone follow-up, as well as social support (136). Whilst participants enjoyed the telephone

follow-up and feedback, they perceived no difference in this being provided by a GP or stroke nurse. Thus the plan for a future roll out of this intervention would be to have only stroke nurse telephone follow-up.

Acceptability of the intervention

From the recruitment and adherence rates it can be seen that the intervention and study protocol were acceptable to participants. It would have been interesting to elicit the views of the 81 eligible patients who never consented to telephone contact from the researcher as well as the 4 who never entered the study, but ethical approval was not given to do this. Acceptability of the intervention was also assessed qualitatively through focus group work and it can be seen from participants' and stroke nurses' comments that the intervention and research assessments were positively received.

Previous authors (264) have reported that having a qualitative aspect to research, "investigating the beliefs, attitudes, needs and situation of the people who will be using the intervention", allows the intervention to be "more relevant, persuasive, accessible and engaging". This person-based approach has been at the heart of the development process for this complex health service intervention, with patient involvement throughout the whole process, including forming a patient and public involvement (PPI) group, which has helped with the acceptability of our intervention.

Sample size calculation

Forty participants were recruited to the pilot study although I had initially hoped for 60 within the allocated time frame. However, a sample of 40 provides sufficient data to

allow a sample size calculation for a definitive randomised controlled study of the intervention, based on the primary outcome measure of a reduction in systolic blood pressure. Systolic blood pressure has been selected because it is the most important risk factor for stroke (34) as well as it having been ranked unanimously as the most important outcome measure by the PPI Group. A clinically important reduction in systolic blood pressure of 10 mmHg has been shown to reduce the risk of future strokes by a third (206), with bigger reductions in blood pressure showing greater reductions in stroke risk. Based upon a standard deviation of the change in systolic blood pressure of 19 mmHg at 12 weeks of follow-up (taking an average of change from across the 3 groups in the pilot trial), a sample size of 60 in each group is sufficient to detect a difference in the change in systolic blood pressure of 10mmHg between the intervention and control groups with over 80% power and α =0.05. This sample size calculation allows for a 10% drop-out rate and this reduction in blood pressure is similar to that seen in Group 2 of the pilot study. However I recognise that a 10mmHg reduction in systolic blood pressure is optimistic. I have therefore re-run the power calculation with a reduction in systolic blood pressure of 3.6mmHg as per Deijle et al (147) who used lifestyle interventions in post-TIA and stroke patients, with the same standard deviation of the change in systolic blood pressure of 19mmHg at 12 weeks of follow-up, with 90% power and α =0.05, I would need 651 in each group, allowing for a 10% drop-out.

An alternative to this sample size calculation would be to use the Minimal Clinically Important Difference (MCID). The MCID has recently been reported to be 1.1 – 1.5% for safe acute ischaemic stroke treatments (265). An alternative to a sample size calculation based on improvement in systolic blood pressure could be an improvement in quality of life, as measured by the EQ5D-5L index score. The MCID for EQ5D-5L

index score in stroke patients undergoing rehabilitation has been recently shown to be 0.1 (266). However the best approach to the sample size calculation could be explored further with the PPI group and then a revised sample size calculation undertaken if required.

Cost and duration of the intervention

No economic assessment has been conducted as part of this study. However I have begun to collect data that would inform this in a future randomised controlled trial and will be reported as per the CHEERS guidelines (267) as well as other authors who have recently published in this area (268). Information to collect will include cost of printing the manual, cost of a stroke nurse telephone contact (band 6 nurse), number of future vascular events, number of health contacts per participant and length of any hospital admissions. The current study duration was 12 weeks but the plan for future trials would be to extend this to 6 months as per the qualitative feedback.

Outcome assessments

Data collection was generally successful although could clearly be improved for disabled participants. For example one participant in a wheelchair did not have recorded data for several variables, including height, weight, 2MWT performance and TUGT. Exercise interventions, similar to '*The Healthy Brain Rehabilitation Manual*', in those with chronic diseases, including post-stroke, can improve functional capacity, reduce disability and improve quality of life (151). Thus one measure to consider including in the next stage of this intervention's development is functional capacity,

which can be measured via the SF-36 Physical Function Scale (269) and this measure can be completed by wheelchair users. I will also review the need for additional equipment to measure height and weight within this patient group. Rather than the 2MWT exercise performance measure I will consider the use of the 6 minute wheel test for wheelchair users as per previous authors (270)(271).

Five of the 28 (17.86%) patients who received a pedometer lost it during the study. Three other participants also felt that the step count was under-estimating the amount of physical activity which they were doing, with a further one participant discontinuing their pedometer use due to waist line irritation and another patient could not use it as they were in a wheelchair. Although pedometers have been reported to be feasible for use in stroke patients, their accuracy at slow walking speeds has been questioned (90)(91) and this appeared a particular issue with the more frail participants. Despite this, positive experiences with using pedometers were reported in the feasibility study (272) and in previous community-based physical activity research that I have been involved in (209). For the next stage in the development of the intervention, I will therefore explore alternatives to pedometers, such as a wrist-worn physical activity device, testing this out within a further internal pilot study.

The intervention found a statistically significant reduction in systolic blood pressure in Group 2 (137.9 (SD 16.36) at baseline to 127.6 (SD 9.95) at follow-up). Although this is a pilot study, these results indicate the potentially positive impact that this intervention can have on reducing systolic blood pressure and other cardiovascular risk factors. Indeed a recent systematic review assessing the effect of lifestyle interventions following a TIA or ischaemic stroke (147) found a 3.6mmHg reduction in systolic blood pressure. Systolic blood pressure is one of the most important risk factors for stroke (34) and a 10 mmHg reduction in systolic blood pressure has been

shown to reduce the risk of future strokes by a third (206), with bigger reductions in blood pressure showing greater reductions in stroke risk.

The intervention promotes adherence to the physical activity guidelines, including the endurance, strengthening and balance components. Indeed the self-reported physical activity questionnaire data and the TUGT and 2MWT performances in Groups 2 and 3, as well as the accelerometer data in Group 2, show that participants increased their general physical activity levels. This is an important finding as a Cochrane Systematic Review which was updated in 2016 (273), has shown that cardiorespiratory and mixed exercise training were effective in reducing disability in stroke survivors. Promotion of walking was also found to be particularly effective at increasing mobility in the stroke survivors and the authors (273) found that a variety of forms of physical fitness training were safe for the stroke survivors to do, in-keeping with the safety findings in the present study.

The positive effects of cardiac rehabilitation on cardiovascular risk factors have been well reported by other authors. Indeed Dalal et al (161), in a review article focused on myocardial infarction, cardiac revascularisation and heart failure patients, reported that cardiac rehabilitation reduces overall mortality (relative risk 0.87 (95% CI 0.75 – 0.99)), cardiovascular mortality (relative risk 0.74 (95% CI 0.63 – 0.87)) and hospital admissions (from 30.7% to 26.1%) with improvements in depression, anxiety and hostility scores. They also reported improvements in systolic blood pressure, serum cholesterol, weight and quality of life measures (161) and these findings have now been supported by my pilot study findings in TIA and ‘minor’ stroke patients.

Participants in the focus group suggested including an assessment of cognitive function within the research programme. Previous authors have reported that in patients aged 45-65 years of age, over one third will have impairment in one cognitive domain 3 months following a TIA (274). A recent systematic review has also shown that exercise can improve cognitive functioning in the over 50s, regardless of baseline cognitive functioning (275) and a small intervention study has shown that aerobic exercise in those with mild cognitive impairment can improve executive functioning (276). To assess cognition, I would therefore propose to use the Montreal Cognitive Assessment (277) tool, which has been previously used in TIA and 'minor' stroke research (278).

The focus group feedback also suggested the addition of a food diary to the manual. Indeed previous work (279) has reported the telephone use of a food diary, with important reductions in cardiovascular risk factors. Higher adherence to a Mediterranean diet is associated with lower ischaemic stroke risk (280) and food diaries improve adherence to the Mediterranean diet (281).

Accelerometer and Physical Activity Measures

Accelerometry is an objective measure of physical activity. Doherty et al (252) showed that wrist-worn accelerometer was acceptable to patients with a high rate of compliance and this is supported within this current study by the high rate of completion of accelerometry assessments. Sedentary time is an important predictor of mortality (282)(283) and inversely associated with healthy ageing (284) and mortality (285). It is therefore important, particularly amongst TIA and minor stroke patients who are at high future cardiovascular risk, to not only educate patients about doing

more physical activity and exercise but also to spend less time sitting. Sedentary time, as objectively measured by accelerometry, reduced in Group 2 at follow-up and this is an important health measure that should be promoted to these patients. Moreover Keadle et al (286) did an analysis on over 100,000 older adults aged 50 – 71 years of age who were part of an NIH cohort study. They found that those adults who watched 5 or more hours/day of TV had a 28% higher risk of death over 6.6 years of follow-up than those who watched less than 3 hours/day. The current intervention appeared to reduce sitting time, as measured by the IPAQ, with fewer adults spending 5 or more hours sitting per day at follow-up compared to baseline, albeit that this was a self-reported measure.

Group 2 improved their objectively measured moderate and moderate-vigorous physical activity at follow-up as measured by the accelerometer. The American Heart and Stroke Associations have produced physical activity and exercise recommendations for stroke patients (109). In keeping with the guideline recommendations, '*The Healthy Brain Rehabilitation Manual*', supports the use of tailored physical activity goals and exercise prescription, which should help promote long-term adherence (109).

Bohannon et al (287) report that the mean 2MWT performance for adult men is 189.4m and for adult females it is 176m. The results for the current study participants are below this. Thus although the intervention improved 2MWT performance at follow-up compared to baseline, further improvement could be achieved and a longer term intervention with an appropriate exercise prescription is planned for the next stage of the research process. The authors (287) also reported that the test-retest intraclass correlation coefficient of the 2MWT was 0.82, thus helping to ensure that the present results are reliable when comparing baseline to post-intervention values.

At follow-up the mean increase from baseline in steps/day in Group 2 was 1,164 and 1,885 in Group 3 and this was similar to the increase in steps/day found in the feasibility study (272). Cupples et al (243) used a pedometer in 45 patients finishing a supervised 8-week, hospital-based cardiac rehabilitation programme to try to maintain physical activity levels. After 6 weeks of follow-up in the pedometer/intervention arm, they found a mean increase in steps/day of 2,742 from baseline. Their mean steps/day was 6,132 at baseline and 8,352 at the 6 weeks of follow-up, which is comparable to the baseline and follow-up results for Group 3. Participants in their study enjoyed having a step-count goal/target to achieve, a finding supported within our qualitative findings as well as national guidelines (136). Also in accordance with my findings, 5 of their participants felt it was under-recording and 2 had issues positioning the device on their clothes, although none reported losing it. However the pedometer step counts for Groups 2 and 3 in the present study do not seem to correlate with the accelerometry data, with only Group 2 improving their moderate-vigorous physical activity levels at follow-up. This finding may be partially explained by the pedometer dropouts, with the included pedometer values perhaps inflating the true response in Group 3.

Previous authors (288) have compared self-reported sedentary time to objectively measured sedentary time and found that self-reported tools generally underestimated sedentary time. This is generally comparable to my findings. However I advised my study participants to wear the accelerometer throughout the day and sedentary time values are therefore high, as they include sleep periods.

Stroke risk post-TIA

In this study of 40 patients with 12 weeks of follow-up after a TIA or minor stroke, only 1 patient, who was in the control group, had a further event. This event was diagnosed as an ischaemic stroke. Coull et al (9) in their Oxford, United Kingdom, primary care based study estimated the risk of stroke after a TIA in the first 90 days as 17.3% (95% confidence interval 9.3 – 25.3%) and the risk of stroke following a minor stroke as 18.3% (95% confidence interval 10.3 – 26.7%). Although this is a pilot study, the reduction in cardiovascular events reported in this study suggests that, '*The Healthy Brain Rehabilitation Manual*', is an effective form of secondary prevention to use in the acute period following a TIA and/or minor stroke. The safety of this approach is supported by the evidence from the systematic review in Chapter 2 (179), which found no excess deaths in those undergoing rehabilitation compared to controls, in keeping with the findings in the feasibility study described in Chapter 5 (272).

Chronic symptoms following a TIA and/or 'minor' stroke

Despite TIAs being described as 'transient', previous work (186) has shown that post-TIA patients experience prolonged symptoms, for example fatigue and mental health issues as well as ongoing focal neurological symptoms. The authors (186) also report that the TIA patients were keen to learn further information about their condition and appropriate treatments but were left frustrated by the lack of information in this area. My qualitative findings from the patient focus group support the ongoing nature of symptoms following a TIA and/or 'minor' stroke, with fatigue, anxiety, stress, hoarseness, word finding difficulties and cognitive slowing all being reported. This intervention, '*The Healthy Brain Rehabilitation Manual*', with follow-up from a health

professional (GP or stroke nurse) gives people information about these symptoms and gives them suggestions for treatment, helping to fill this current knowledge void.

Protocol components

As can be seen from the above presented qualitative and quantitative results, the protocol worked well although some improvements have been suggested for the next stage of the trial and these have been included within the implications for future work section (see below). Indeed Greaves et al (289) undertook a systematic review of reviews to identify the effective components of programmes that are associated with the greatest change in physical activity levels and dietary improvement in those patients at risk of type II diabetes mellitus. Similar to this current work, they found that effectiveness was improved by facilitating social/family support (which is actively encouraged within our manual), targeting both diet and physical activity promotion together, increased review contacts and using appropriate behaviour change techniques (as described in Chapter 5 for our intervention), such as goal setting, feedback, reviewing goals and self-monitoring. Adding social/family support also appeared to promote a longer term (12 months in this review) improvement in results. Moreover a recent systematic review and meta-analysis reviewing the effect of lifestyle interventions post-TIA and/or stroke (147) suggested that future randomised controlled trials investigating the effect of lifestyle interventions on preventing cardio- and cerebro-vascular events, mortality and cardiovascular risk factors should meet 5 criteria:

a) complete description of the intervention;

b) the intervention should have more than 8 contact moments over more than 4 months;

c) the intervention should use greater than 3 behaviour change techniques;

d) the intervention should focus on physical activity and exercise promotion as well as managing the other modifiable cardiovascular risk factors;

e) a theoretical framework should be used in developing the intervention.

'*The Healthy Brain Rehabilitation Manual*' currently meets 4 out of these 5 criteria and for the next stage of the intervention development, the plan is to increase the duration of follow-up beyond 3 months, allowing more than 8 contact moments, therefore ensuring all 5 criteria are met. Thus the intervention and research methods are in keeping with the current evidence base for secondary cardiovascular prevention in this patient cohort.

Implications for future work

The proposed intervention has the potential to reduce future cardiovascular risk in those patients experiencing a TIA and/or 'minor' stroke. There is a high level of interest currently amongst stroke health professionals and commissioners about how to effectively implement non-pharmacological secondary prevention post-TIA and/or 'minor' stroke (14). If strong evidence of the effectiveness of such interventions can be found within a randomised controlled trial, then they should be implemented for this patient population throughout the UK.

For the next stage in the development of the intervention, I am planning to:

- Add SF-36 (269) and the Montreal Cognitive Assessment (277) tool to the study measurements.
- I am also hoping to recruit directly from the TIA and 'minor' stroke clinics so that patients do not have to return on a different occasion to get enrolled in the research.
- Follow-up will be extended to 6 months with monthly follow-up calls and the 2 intervention arms will reduce to 1, with only stroke nurse telephone follow-up. Further training is planned for the stroke nurses on the use of physical activity monitors during follow-up.
- I will add a section at the start of the manual asking patients, "What matters to you?" (290) to help encourage a more open approach at the health professional contacts and develop an electronic version of the manual following patient feedback, as well as trialling alternatives to pedometers and including a food diary for use in the manual.
- There will also be further space within the manual to write questions to ask health professionals and a section added to the physical activity chapter on how to exercise during the winter months and periods of bad weather.
- I will also apply for ethical approval to have access to the participants' electronic healthcare record for the next study.

Strength and Limitations

The main strength of this study is the use of rigorous research methods in piloting the intervention and assessing the feasibility of conducting a full-scale randomised

controlled trial (246). Physical activity was assessed objectively using accelerometry and blood pressure was measured using BpTru, which is equivalent to 24 hour blood pressure monitoring (218), the current national UK standard for diagnosing hypertension (291). I also recruited patients from across a broad range of socio-economic deprivation levels, as well as from across educational attainment levels, with most recruits only being educated up to secondary/high school level. This pilot study also recruited from across NI, with only the Western Trust not recruiting, therefore allowing me to test if this is a feasible intervention to deploy throughout the region. The recruitment rates were very favourable for a pilot study and could have improved if a further 3 eligible patients had been given an invite into the study. Recruitment could also have been improved by having a dedicated Research Stroke nurse in all sites. Another strength is the low study drop-out rate. Due to the randomisation process the study groups were well-balanced in terms of their baseline measurements and the nurse doing the follow-up assessments was blinded to study group allocation as well as the statistician being blinded to group allocation.

Only white, English speaking people were included in the study. Therefore to help improve the generalisability of the study findings, I would hope to recruit from across ethnic population groups. I would plan to achieve this by recruiting across NI and holding regular 'cardiovascular prevention' clinics in every hospital to capture suitable patients. The study measurements were not adapted for a study participant in a wheelchair and for the next stage in the intervention's development, I therefore plan to include measurements, which could be undertaken for disabled participants. From reviewing the baseline data there was a preponderance of TIA patients in Group 2. I plan to ensure an even spread of TIA and 'minor' stroke patients across the control and

intervention arms by using stratified randomisation. Finally, to improve the qualitative review of the intervention, I would hope to ask about the views of those not entering the study regarding recruitment and I will apply for appropriate ethical approval to do this.

Conclusion

This pilot study of an innovative secondary prevention intervention, '*The Healthy Brain Rehabilitation Manual*', utilising core components of home-based cardiac rehabilitation in those suffering a first TIA or minor stroke within the preceding month, has shown that a randomised controlled trial to test its effectiveness is practical, that high recruitment and retention rates are possible, and that the intervention and trial is acceptable to patients. '*The Healthy Brain Rehabilitation Manual*' is a patient-centred rehabilitation programme and has shown potential in reducing important cardiovascular risk factors in a patient cohort who are at high cardiovascular risk. Subject to some minor changes to the intervention, the addition of new outcome measures and longer-term follow-up, the intervention is now ready for evaluation in a full-scale randomised controlled trial. If this trial demonstrates statistically significant results, then implementation of this intervention into clinical practice would ensure that UK health trusts achieve the recently published national guidelines for TIA and stroke management (14). Indeed the intervention provides an appropriate rehabilitation and secondary prevention programme for TIA and 'minor' stroke patients, as well as appropriate guidance for patients regarding return to work, a supportive early discharge model, better management of systolic blood pressure (to aim for less than 130mmHg) and the promotion of 'life after stroke'. Thus this

intervention has the potential to significantly improve the management of TIAs and ‘minor’ stroke whilst ensuring adherence to national UK treatment guidelines.

Chapter 7

Personal Reflection and Implications for Future Practice

Personal reflection

Through my PhD I have gained lots of invaluable skills. Firstly, going through the process of obtaining external NIHR PhD funding was taxing but has equipped me with the necessary skills I hope for a future clinical-academic career – in particular, how to persevere and change an unsuccessful funding bid into a successful one. I have enjoyed the teamwork and leadership skills required to undertake a successful research programme and would hope to further develop these skills through further research work. In particular, I am looking forward to utilising technology to help improve the efficiency and user experience of my research project.

There was a considerable amount of time and effort required to obtain all the necessary ethical and clinical governance approval for the studies, particularly as I was working across 4 trusts. The ethical and clinical governance approval processes should ideally be streamlined with a view to avoiding duplication of work across Trusts.

Through the PhD I have successfully developed a complex health service intervention following appropriate guidelines and putting the patient experience and views at the heart of this. As well as developing this intervention further, I would hope to utilise these skills in developing complex health service interventions in other medical fields, helping to improve patient care.

Implications for practice/future research

I would like to complete the steps in developing a complex health service intervention, by applying for funding to do a randomised controlled trial, to test the effectiveness of the '*The Healthy Brain Rehabilitation Manual*', powered to detect reductions in systolic blood pressure. I would also like to offer a regular secondary cardiovascular prevention service to those patients experiencing recent cerebrovascular events as well as other high risk vascular patients ('panvascular rehabilitation programme'). To enable me to do this I would like to develop the manual into an app to be downloaded onto a smartphone. I could then offer patients the option of having the paper copy of the manual or the electronic app version. I would also be keen to expand the different options available to patients to improve their cardiovascular risk, particularly in terms of alternatives to pedometers. Moreover, I would be keen to work with community-based organisations to ensure my rehabilitation programme fits the needs of service users and what they as organisations can offer patients. Indeed some patients may wish to benefit from running/jogging classes whilst others may wish to attend cooking classes to teach them about the Mediterranean diet and how to prepare appropriate meals, for example. These may be interventions that could be offered by local charities, for example NI Chest Heart and Stroke, and could complement '*The Healthy Brain Rehabilitation Manual*'. Seasonality also affects adherence to physical activity and exercise prescription and one way to account for this would be report weekly average rain fall in the area in which the research participant lives when conducting the next stage of this research study, the randomised controlled trial.

Figures, Tables and Appendices

Figure 1 – Flow diagram of reviewed and included papers for Systematic Review 1 (Rehabilitation Programmes with Secondary Prevention Lifestyle Interventions Initiated within 90 days following a TIA or 'minor' stroke: Systematic Review and Meta-analysis)

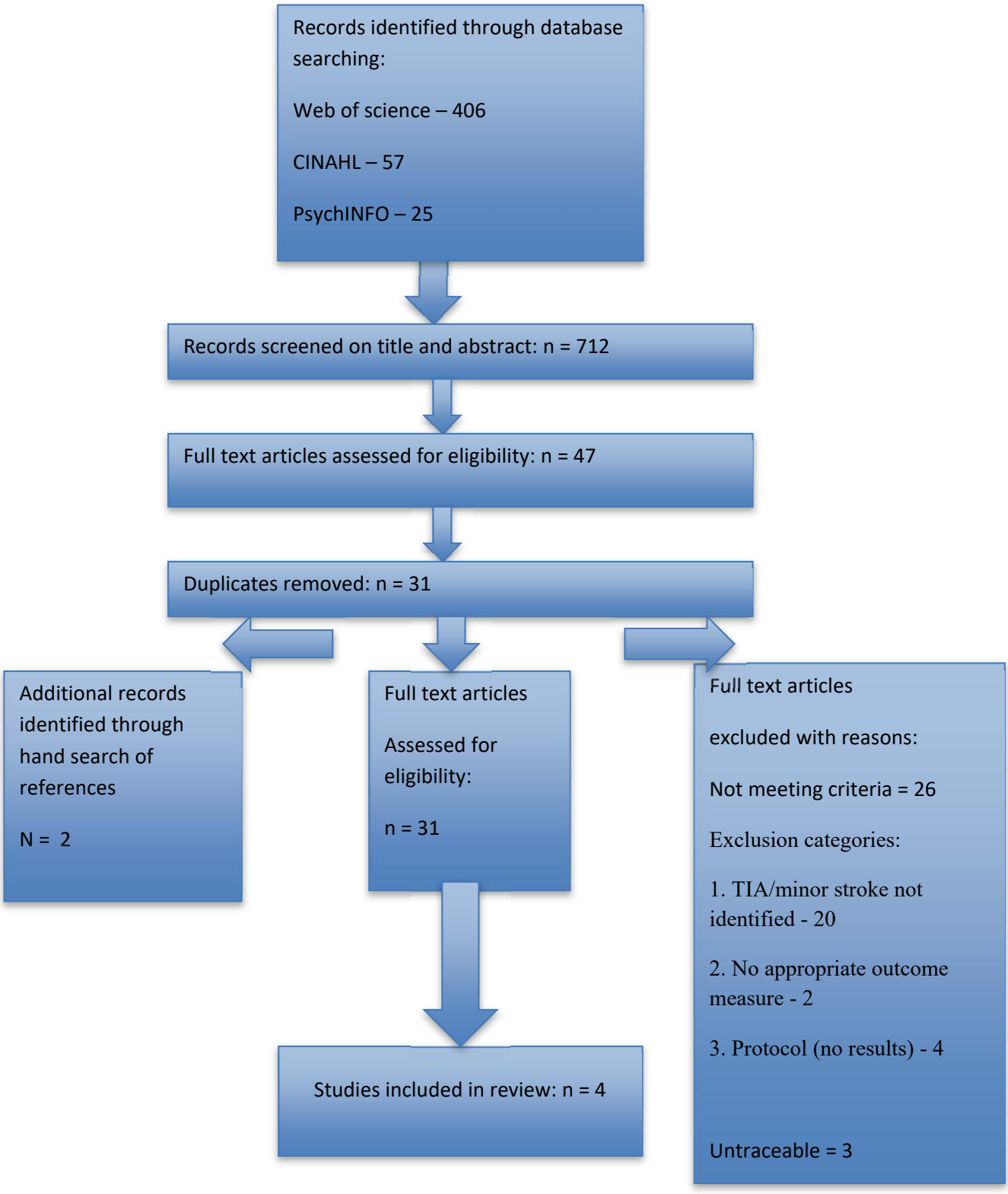

Figure 2 – Resting systolic blood pressure (mmHg) in the experimental compared to the control groups post-intervention for Systematic Review 1 (Rehabilitation Programmes with Secondary Prevention Lifestyle Interventions Initiated within 90 days following a TIA or 'minor' stroke: Systematic Review and Meta-analysis)

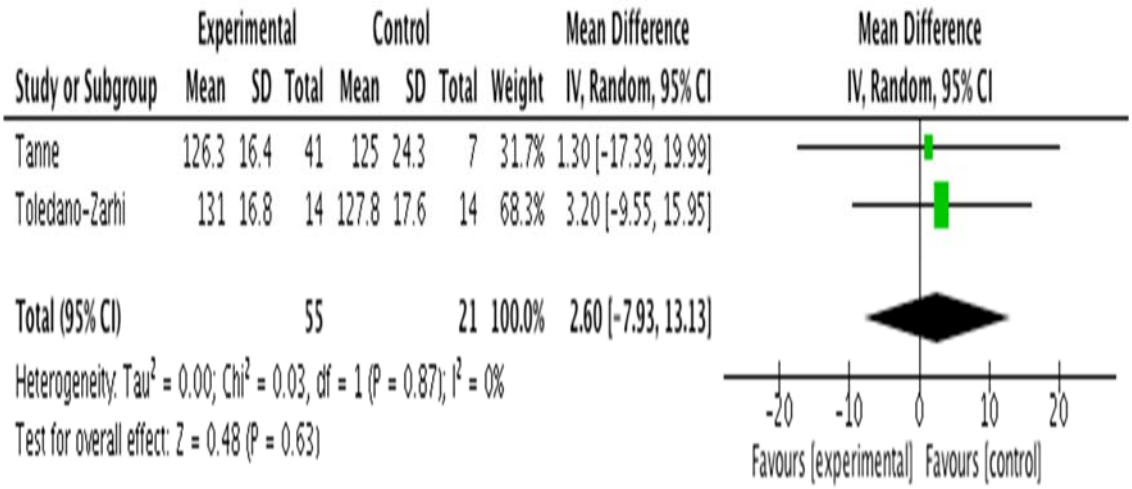

Figure 3 – Six minute walking test performance (metres walked) in the experimental compared to the control groups post-intervention for Systematic Review 1 (Rehabilitation Programmes with Secondary Prevention Lifestyle Interventions Initiated within 90 days following a TIA or 'minor' stroke: Systematic Review and Meta-analysis)

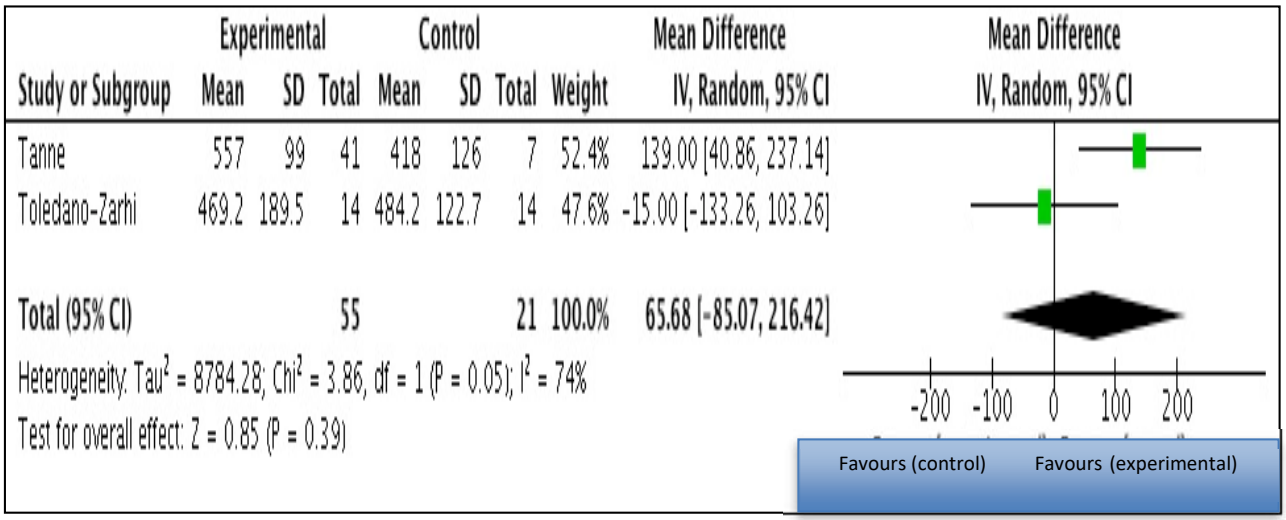

Figure 4 – exercise testing result (METs) in the experimental compared to the control groups post-intervention for Systematic Review 1 (Rehabilitation Programmes with Secondary Prevention Lifestyle Interventions Initiated within 90 days following a TIA or 'minor' stroke: Systematic Review and Meta-analysis)

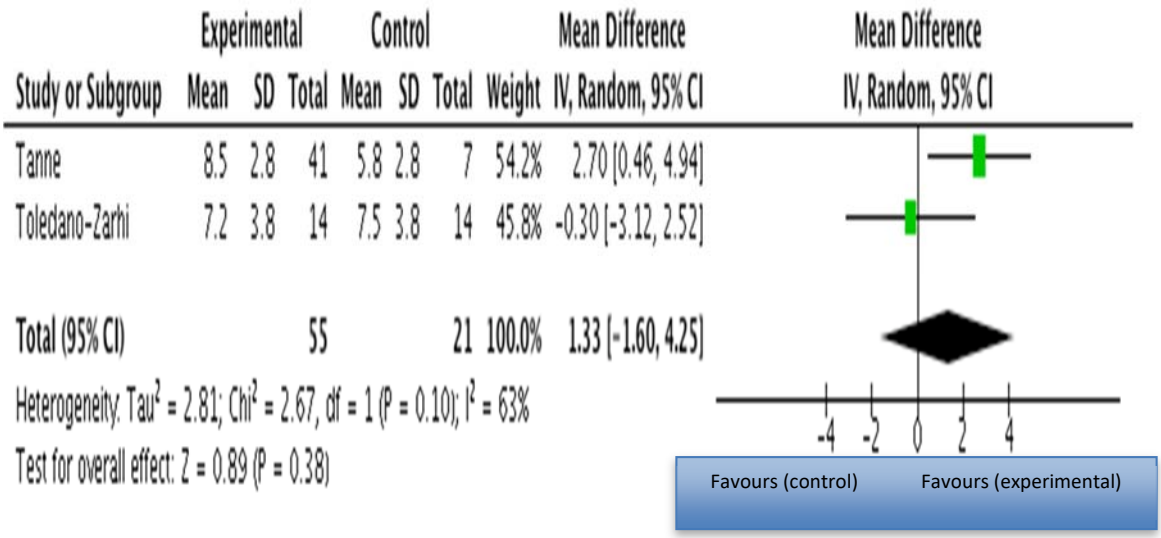

Figure 5 – Flow diagram of reviewed and included papers in Systematic Review 2 (Behaviour change techniques in home-based cardiac rehabilitation programmes for patients with cardiovascular disease: systematic review)

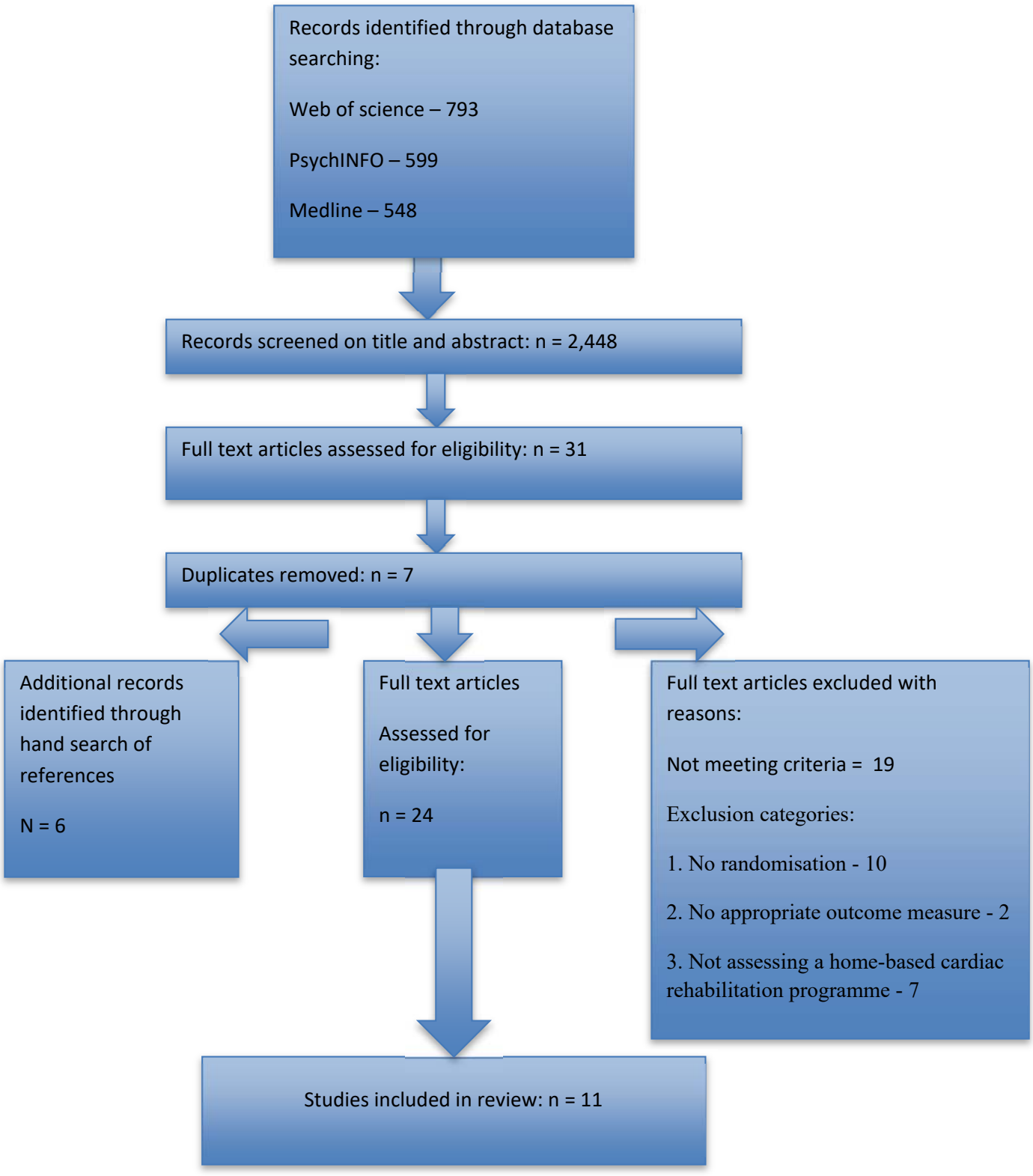

Figure 6

Funnel plot for the variable systolic blood pressure in Systematic Review 2 (Behaviour change techniques in home-based cardiac rehabilitation programmes for patients with cardiovascular disease: systematic review):

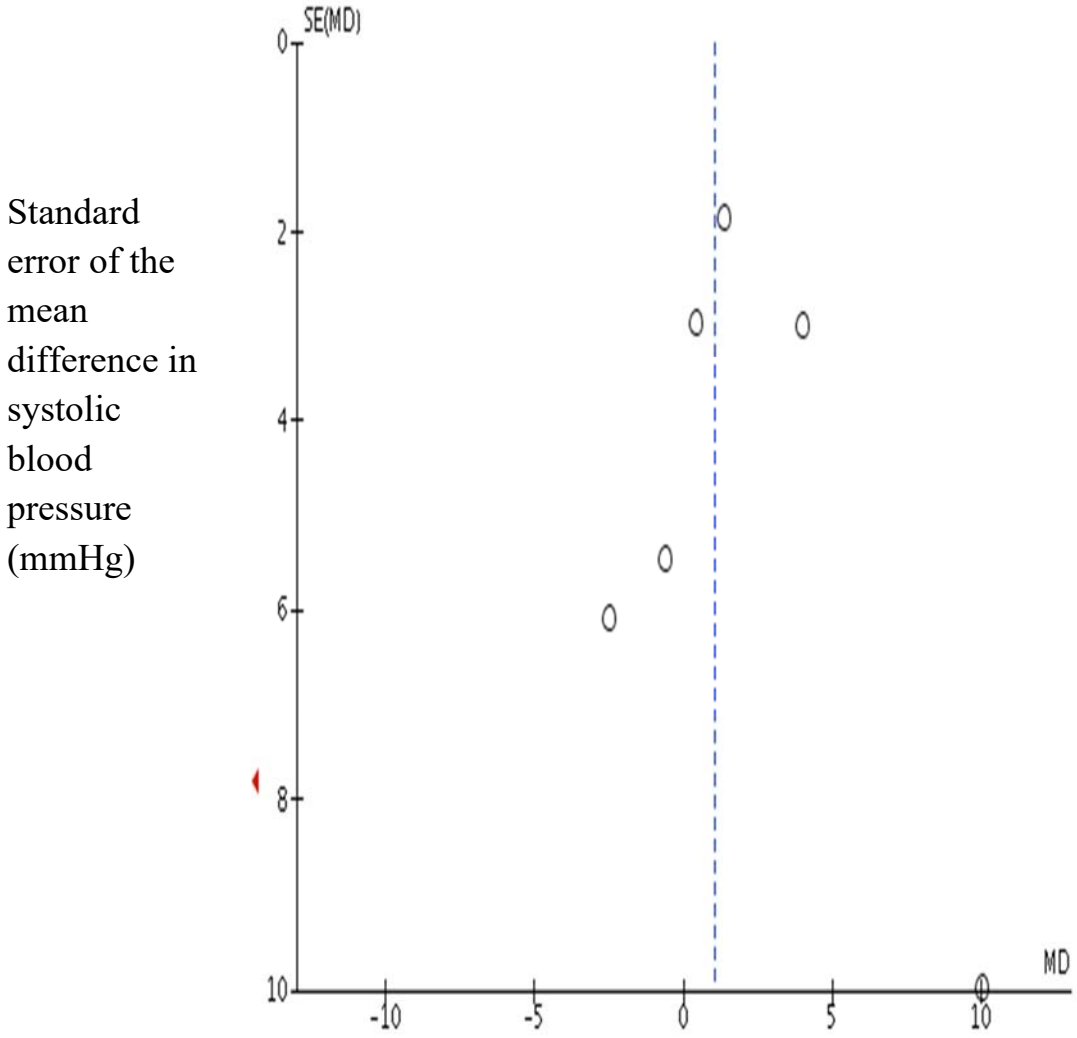

Figure 7

Funnel plot for the variable diastolic blood pressure in Systematic Review 2 (Behaviour change techniques in home-based cardiac rehabilitation programmes for patients with cardiovascular disease: systematic review):

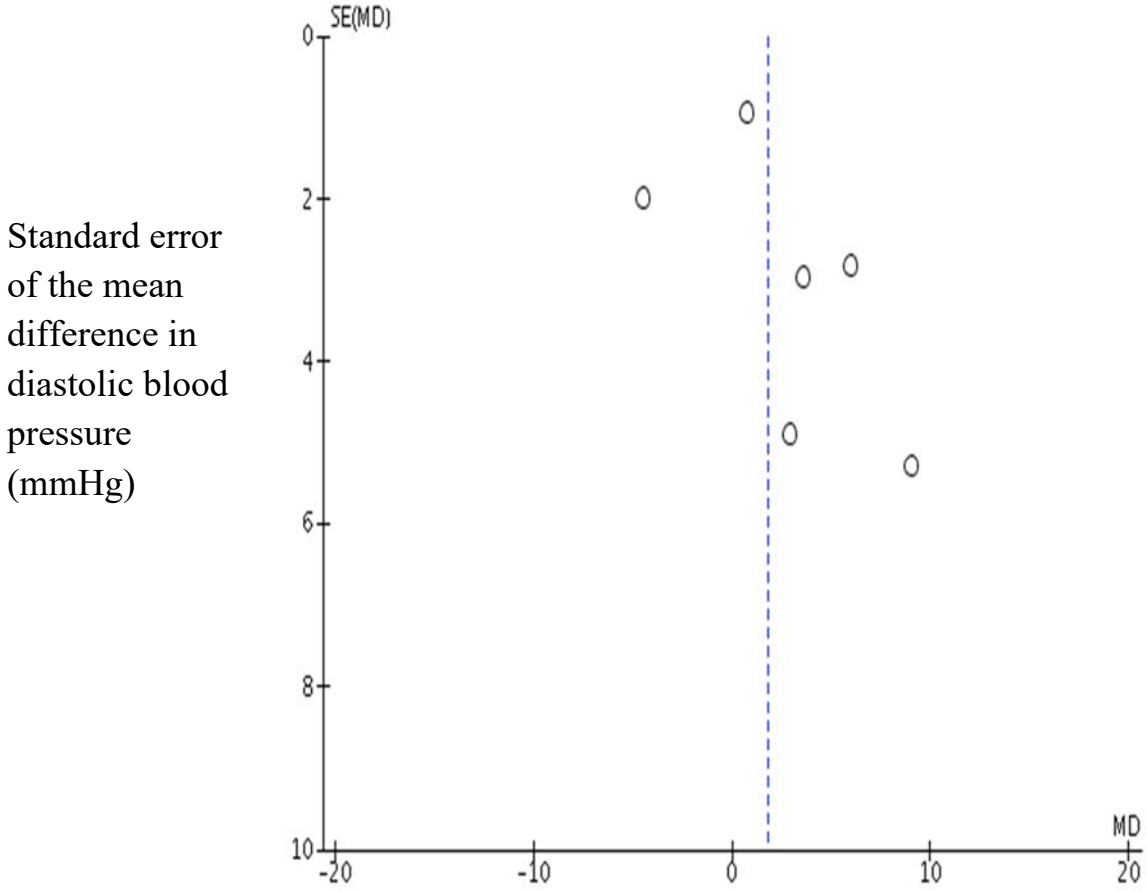

Figure 8

Meta-analysis of resting systolic blood pressure (mmHg) in Systematic Review 2 (Behaviour change techniques in home-based cardiac rehabilitation programmes for patients with cardiovascular disease: systematic review)

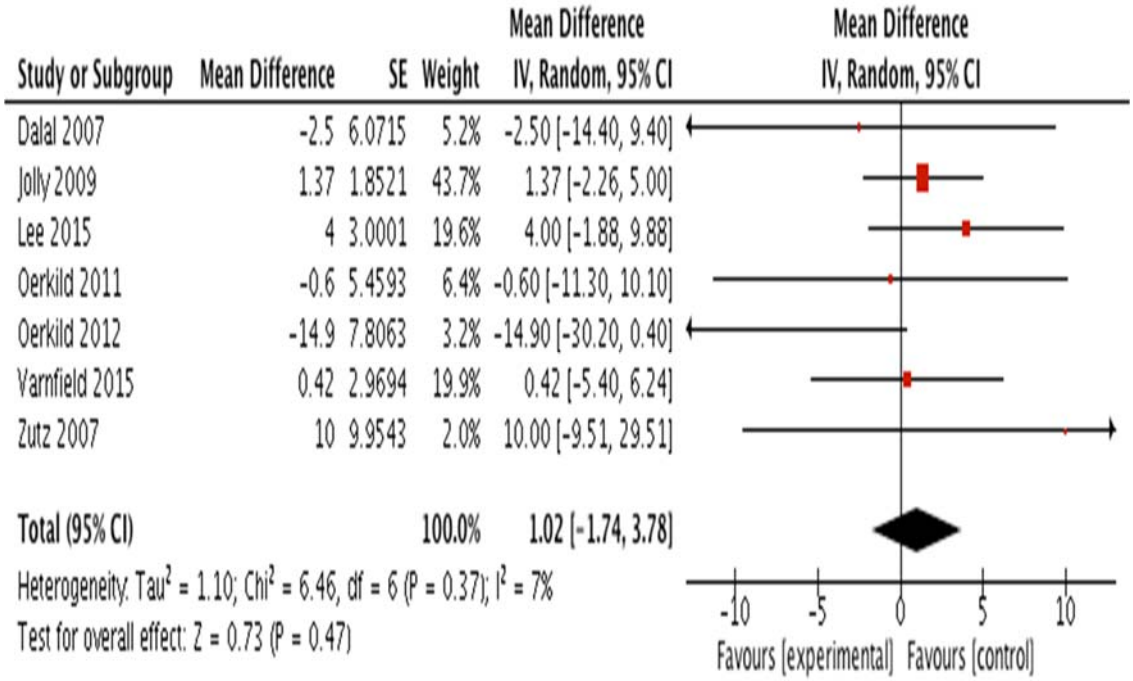

Figure 9

Meta-analysis of total cholesterol (mmol/l) in Systematic Review 2 (Behaviour change techniques in home-based cardiac rehabilitation programmes for patients with cardiovascular disease: systematic review)

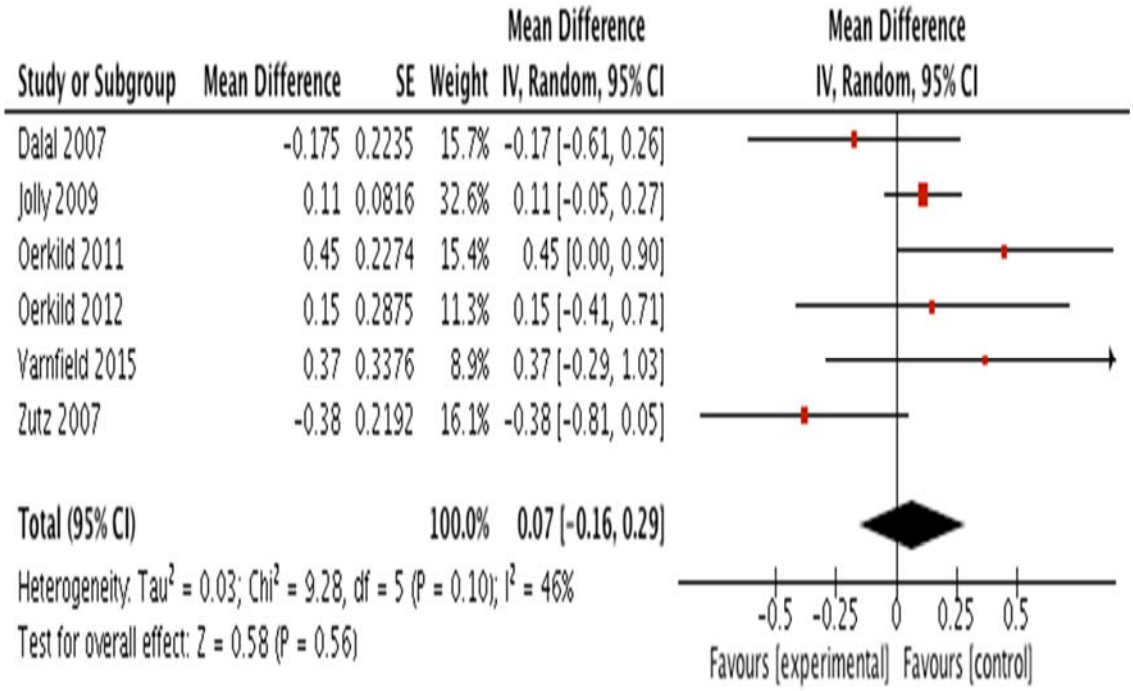

Figure 10

Meta-analysis for the anxiety section of the HADs questionnaire in Systematic Review 2 (Behaviour change techniques in home-based cardiac rehabilitation programmes for patients with cardiovascular disease: systematic review)

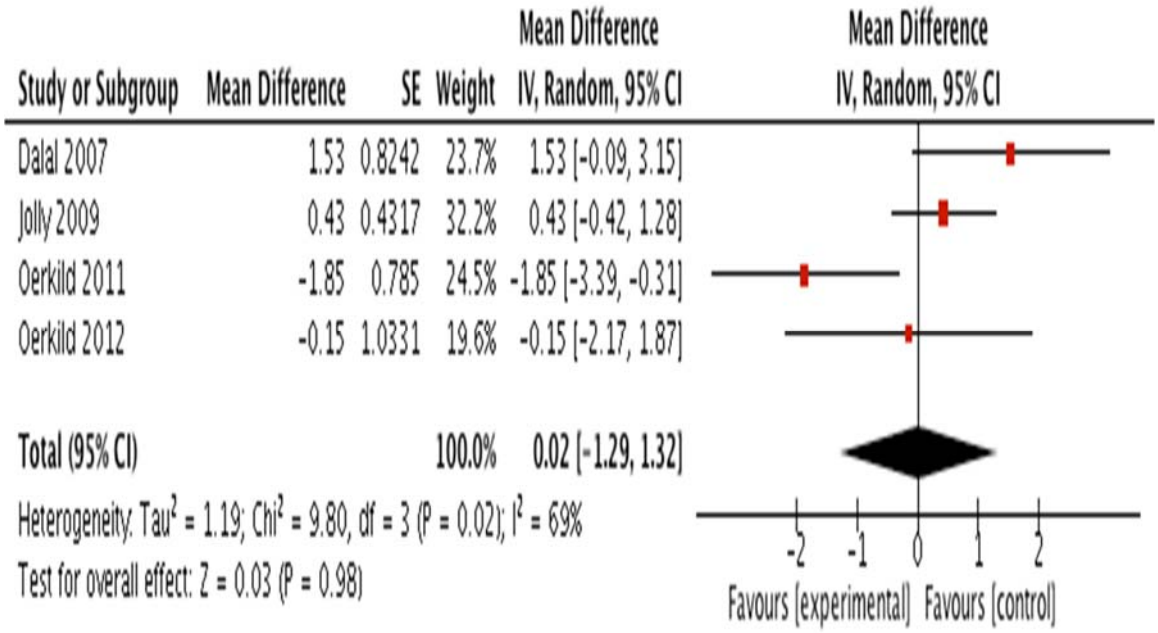

Figure 11 Intervention Logic Model for the Feasibility Study

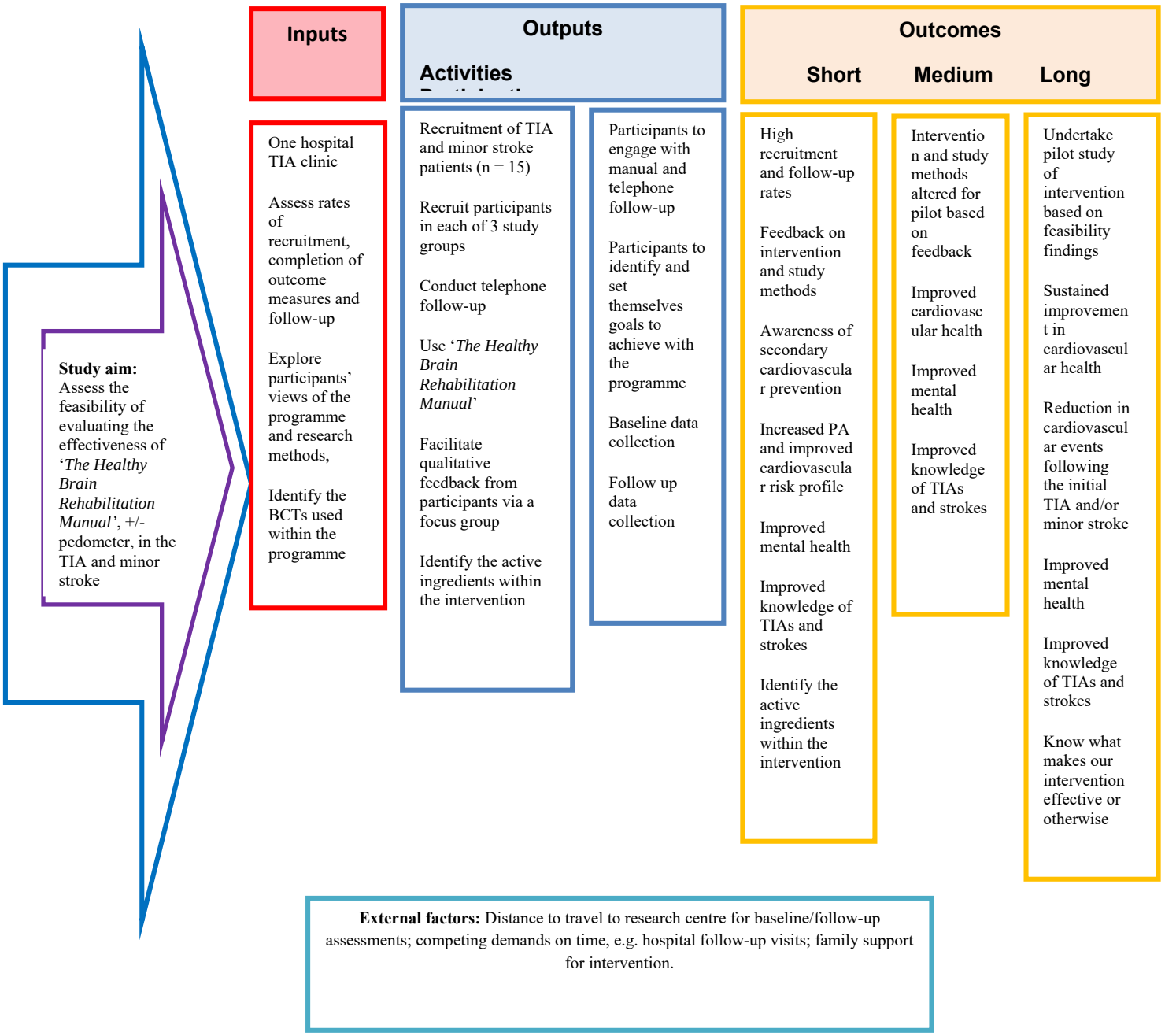

Figure 12 - CONSORT Flow diagram for Pilot Study

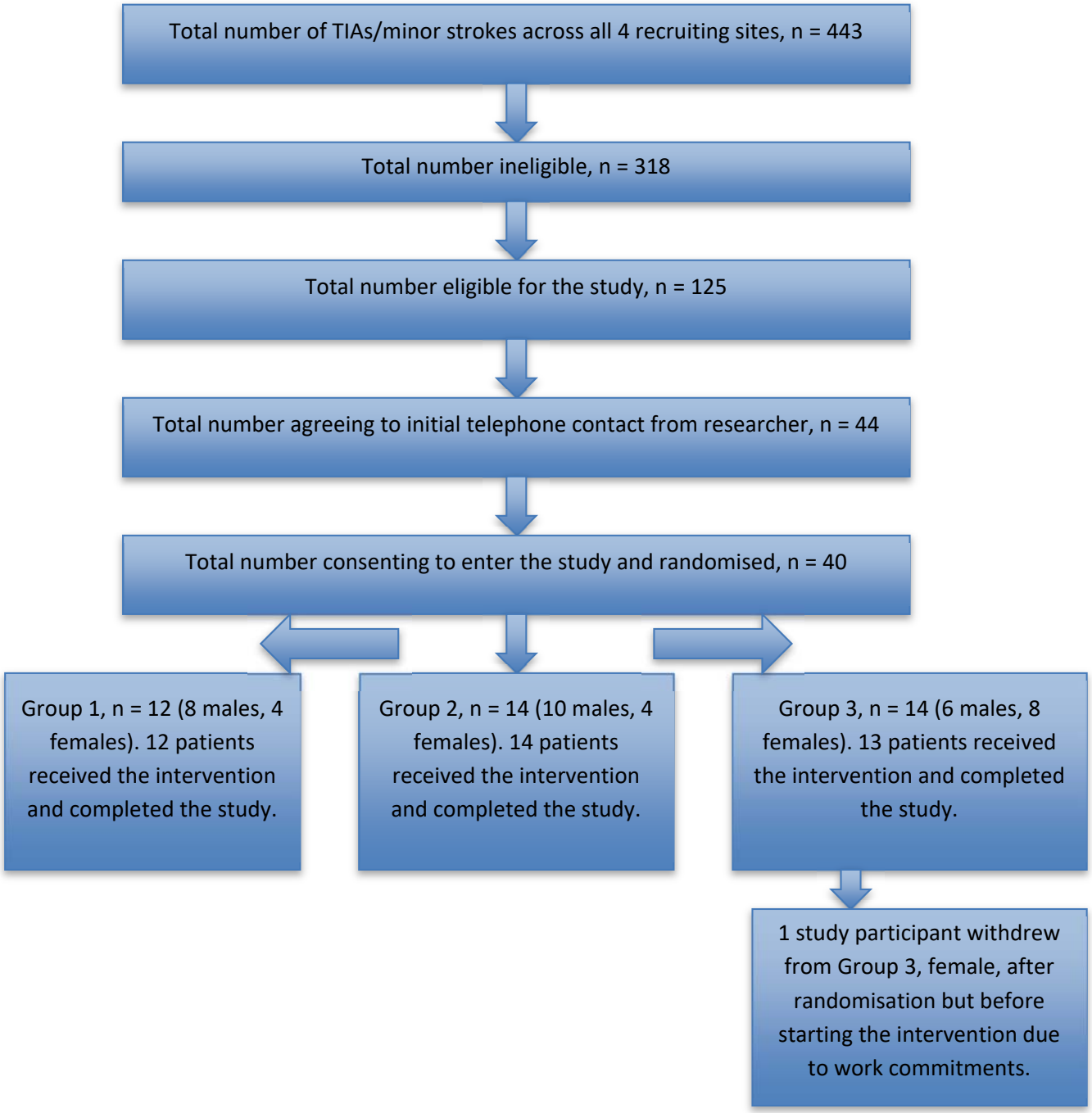

Table 1 – Information on included studies, Risk of Bias and PEDrO Score

Study	Sample size	Dropouts	Intervention design	Follow-up duration	Control	Risk of bias
Allen et al. 2009. (142)	Intervention (I) 190; Control (C) 190	I: 25 C: 36	Comprehensive post-discharge care management intervention; assessment by nurse in participants' home; reviewed by the treating medical team. Patient care plans developed. Periodic telephone calls to assess change.	6 months	Usual post-discharge care planning.	Low
Tanne et al, 2008. (145)	I: 43 C: 9	I: 2, C: 2	Education on vascular risk, physical exercise and healthy lifestyle; supervised exercise program, twice/week for 3 months (15 mins warm-up, 45 mins on treadmill, stair machine and bicycle at 60-70% of maximal heart rate); prescribed by physiologist; supervised by physical therapist and cardiac rehabilitation staff. Exercise prescription adjusted if capacity improved.	3 months	Usual post-TIA/stroke care.	High. Pilot non-random trial
Toledano-Zarhi et al, 2011. (143)	I:14, C: 14	I: 1, C: 0.	Exercise group enrolled in 6-week supervised exercise program - 3 hours weekly: 2 sessions of 35-55 mins on treadmill, hand-bike and bicycle, supervised by physical therapy and cardiac rehabilitation staff: 8 progressive stages; also, 45-55 mins group practice for strength, flexibility and coordination. Exercise prescription adjusted if capacity improved.	6 weeks	Home-exercise booklet, advising strength and flexibility exercises, plus normal routine	Un-certain

					care.	
Boysen et al. (144)	I: 157, C: 157	I: 24, C: 14	Repeated encouragement and verbal instruction on being physically active given by a physiotherapist or neurologist.	2 years	Verbal information on benefits of physical activity	Low risk

Table 2 – BCTs used by the included studies

BCT Label	BCT group	Example of how the BCT was used	Studies using BCT (N; references)
Instruction on how to perform a behaviour	Shaping knowledge	"education regarding lifestyle modification" (142)	4; (142) (143) (145) (144)
Goal setting (behaviour)	Goals and planning	"… exercise at "60-70% of maximal heart rate, as prescribed by a physiologist" (145)	3; (143) (145) (144)
Action planning	Goals and planning	".. twice weekly session of 35-55 minutes on a treadmill, a hand-bike machine and a bicycle. ……. A pulse rate target of 50-70% of maximal heart rate…" (143)	2; (143) (144)
Credible source	Comparison of outcomes	"The experimental intervention consisted of repeated encouragement and verbal instruction on being physically active given by a physiotherapist…." (144)	2; (142) (144)
Monitoring of behaviour by others without feedback	Feedback and monitoring	"Compliance was monitored…" (143)	2; (142)(143)
Review behaviour goal(s)	Goals and planning	Participants were "encouraged to increase efforts and to exercise more…" (144)	1; (144)
Behavioural contract	Goals and planning	"…instructor and participants would fill in a standard agreement form with various choices of physical activity…" (144)	1; (144)
Self-monitoring of behaviour	Feedback and monitoring	"... received a personalized health record to help them self-manage their risk factors." (142)	1; (142)
Social support	Social support	"Considerable effort was taken to motivate the participants."	1; (144)

(unspecified)		(144)	
Social support (practical)	Social support	"…ensure that needed social services (e.g. Meals on Wheels….) were in place…" (142)	1; (142)
Social support (emotional)	Social support	"…intervention to reduce common post stroke complications (e.g. depression…)" (142)	1; (142)
Information about health consequences	Natural consequences	" educated on vascular risk factors and the importance of physical exercise…." (145)	1; (145)
Demonstration of the behaviour	Comparison of behaviour	"…group practice for inducing strength, flexibility and coordination performances" (143)	1; (143)
Prompts/cues	Associations	"…repeated instructions and readjustment of the physical activity plan." (144)	1; (144)
Behavioural practice/ rehearsal	Repetition and substitution	"…group practice for inducing strength, flexibility and coordination performances was performed once a week…" (143)	1; (143)
Pharmacological support	Regulation	'..medication reconciliation and pill organizers to optimize stroke risk factor control." (142)	1; (142)
Adding objects to the environment	Antecedents	"…and pill organizers to optimize stroke risk factor control…." (142)	1; (142)

Table 3 – Information on included studies, Risk of Bias and PEDrO Score

Study	Sample (n)	Drop-outs	Population	Setting	Intervention design	Follow-up duration	Control	Main outcomes	PEDrO score*
Jolly et al, (114)	525	Home programme 6 month data n = 246 (11 DNA, 3 died, 3 withdrew); at 12 months n = 239 (14 DNA, 4 withdrew). Hospital programme 6 month data n = 239 (18 DNA, 2 died, 3 withdrew); at 12 months n = 236 (20 DNA, 1 died).	After acute MI, coronary re-vascularisation or CABG	UK	'Heart manual' for patients covering risk factor management. Telephone follow-up.	12 months.	Hospital-based CR.	Home-based CR comparable to hospital-based CR in CVD risk factor improvements at 12 months of follow-up. Similar costs in running each programme.	9
Dalal et al, (166)	230 – 104 into randomised arm and 126 into preference arm.	9 month follow-up data were available for 84/104 (81%) randomised and 100/126 (79%) preference patients.	Hospitalised for acute MI.	UK	'Heart Manual' for 6 weeks. Cardiac rehab nurse made one home visit in 1st week after discharge followed up by telephone calls over 6 weeks (typically one call in weeks 2, 3, 4 and 6).	9 months	Hospital-based CR	Home-based CR (Heart Manual) as effective as hospital-based CR in improving modifiable CVD risk factors.	8
Zutz et al, (169)	15 – 7 for usual care and 8 for the	2 dropouts by the end of the study for the usual care	On a waiting list for cardiac rehabilitation	Canada	Internet-based intervention with education modules,	12 weeks.	No active treatment.	The home-based CR programme	8

	home-based intervention.	group.	living within 60km of site.		email communication with case manager and dietician, optional on-line discussion group and entry of health behaviour data to monitor self-progress.			group significantly improved their modifiable CV risk factors compared to controls.	
Sinclair et al, (173)	324 – 163 in intervention and 161 in control groups.	134/163 (82%) in intervention group; 133/161 (82.6%) in the control group.	Discharged from hospital with acute MI and aged greater than or equal to 65 years old	UK	At least 2 home visits from trained support staff nurse to encourage patients around compliance, risk factor reduction, advice on stress, exercise, smoking cessation and diet. Visits supplemented by telephone support and manual.	100 day follow-up.	Hospital-based cardiac rehabilitation.	Significant improvement in confidence and self-esteem in the home-based group although comparable improvements in CVD risk factors between home-based and centre-based CR.	8
Lie et al, 2009 (174)	203	93/101 (92%) in intervention group; 92/102 (90%) in control group.	Ischaemic heart disease patients (post-CABG patients).	Norway	A psychoeducation intervention, consisting of structured information and psychological support. All	6 months.	Standard discharge care that involved a non-standardised talk with	Home-based CR comparable to control group in terms of improving	8

					patients in the intervention group received 2 1hr home visits at 2 and 4 weeks after surgery.		the nurse-doctor.	quality of life and activities of daily living.	
Wang et al, 2012 (165)	160	In the intervention group at 6/12 n = 68/80 (85%); for the control group at 6/12 n = 65/80 (81%).	Post-MI patients.	China.	A home-based cardiac rehabilitation programme using a self-help manual, the Heart Manual, developed by the researchers. Patients had a one hour introduction to the manual and telephone follow-up at 3 weeks.	6 months.	Usual care, hospital-based cardiac rehabilitation.	Home-based CR (Heart Manual) improves quality of life and reduces anxiety compared to usual care for post-MI patients.	8
Lee et al, 2006 (167)	81	No data on drop-outs.	Post-MI or coronary revascularisation patients.	UK	The home-based programme is nurse facilitated (with home visits and telephone contact), using the Heart Manual.	3 months	Hospital supervised exercise sessions twice weekly for 12 weeks.	Home- and hospital-based CR showed comparable improvements in haemostatic indices and CVD risk factors.	9
Piotrowicz et al, 2010	152	75/77 (97%) for home-based intervention;	Heart failure patients.	Poland.	Home-based telemonitored rehabilitation based	8 weeks.	Control group: standard	Home-based CR as equally as	8

(170)		56/75 (75%) for the control.			on continuous walking training on level ground; ECHO3 device and a mobile phone (ECHO3 device enabled ECG recording).		interval training on a cycle ergometer. Both groups: trained 3 times a week. All patients and their partners participated in an education programme.	effective as centre-based CR for heart failure patients although better adherence in home-based group.	
Oerkild et al, 2011 (171)	75 patients	30/36 (83%) for home-based intervention; 34/39 87%) for the control.	Patients 65yo or older with ischaemic heart disease patients.	Denmark	For home-based programme, a physio visited twice within a 6 week interval to develop a training programme that could be performed at home and in the surrounding outdoor area. All patients received counselling and medical adjustment from a cardiologist at baseline and after 3, 6 and 12 months.	12 months	The centre-based CR consisted of a 6 week group-based supervised exercise training for 60 minutes twice a week and were encouraged to exercise at	Home-based CR as effective as centre-based CR in improving exercise capacity, CVD risk factors and health-related quality of life.	8

							home.		
Varnfield et al, 2014	120 patients	For intervention n = 46/60 (77%); for control 26/60 (43%).	Post-MI patients.	Australia	CR delivered at home: health and exercise monitoring, motivational and educational materials; weekly mentoring consultations for 6 weeks, via telephone (approx. 15 mins each)	6 months	Traditional hospital-based CR (TCR) - 2 supervised exercise and 1hr educational sessions weekly for 6 wks at one of 4 community centres.	Home-based CR had better uptake, adherence and completion rates than centre-based CR. Comparable improvements in CVD risk factors in both groups.	8
Oerkild et al, 2012 (172)	40 patients	19/19 (100%) for the home-based intervention; 17/21 (81%) for the control.	65 years old or above with coronary heart disease.	Denmark	Physiotherapist in home visits developed individualised exercise programme for home and surrounding outdoor area. Risk factor intervention, medical, physical and psychological adjustments at baseline, 3, 6, 12 mths.	12 months of follow-up and mortality data after 5.5 years	Usual care with no rehabilitation, who declined participation in centre-based CR.	Home-based CR programme group significantly improved 6MWT performance at 3 months compared to controls.	8

*PEDrO score maximum =11

Table 4 – BCTs used by the included studies

BCT Label	BCT group	Example of how the BCT was used	Frequency of use	Studies where found
3.1 Social support (unspecified)	Social support	"…motivational and educational materials to participants via text messages ……" (168)	11	(170)(169)(167) (173)(165)(168)(174) (166)(171)(172)(114)
1.1 Goal setting (behaviour)	Goals and planning	"Exercise targets were at least 30 min of moderate activity…" (168)	10	(170)(167) (173)(165)(168)(174) (166)(171)(172)(114)
11.2 Reduce negative emotions	Regulation	"…relaxation and stress management techniques…." (167)	7	(174)(165)(168)(114) (166) (173)(167)
4.1 Instruction on how to perform the behaviour	Shaping knowledge	"Patients were carefully instructed in the training programme ……." (172)	7	(172)(165)(114)(166) (173)(167)(171)
2.1 Monitoring of behaviour by others without feedback	Feedback and monitoring	"….used a smartphone for health and exercise monitoring…." (168)	6	(165)(168)(114)(166) (167)(171)
2.3 Self-monitoring of behaviour	Feedback and monitoring	"Participants were asked to wear their heart rate monitors.. and upload their exercise data at least twice per week onto the Web site." (169)	6	(169)(167)(165)(168) (166)(114)
2.4 Self-monitoring of outcome(s) of behaviour	Feedback and monitoring	"Each participant was equipped with a smartphone ... with health diary and activity monitoring applications; blood pressure monitor and weight scale." (168)	6	(169)(167)(165)(168) (166)(114)
9.1 Credible	Comparison of	"….monthly ask-an-expert group chat sessions." (169)	6	(170)(169)

source	outcomes			(173)(166)(171)(172)
11.1 Pharmacological support	Regulation	"…….nurse counselled patients ……, giving information on…drug treatment." (166)	6	(167)(165)(174)(166) (171)(114)
5.1 Information about health consequences	Natural consequences	"… simple explanations about coronary heart disease…" (166)	5	(174)(168)(166) (173) (167)
2.5 Monitoring of outcome(s) of behaviour without feedback	Feedback and monitoring	"Regarding risk factor intervention and medical adjustment, the patients consulted a cardiologist at baseline and after 3, 6 and 12 months." (172)	3	(169)(172) (170)
3.2 Social support (practical)	Social support	"…technical phone support during the trial if required." (168)	3	(168) (173) (167)
12.5 Adding objects to the environment	Antecedents	"Each participant was equipped with a smartphone…" (168)	3	(168)(166) (167)
1.2 Problem solving	Goals and planning	"…self-help treatments for psychological problems commonly experienced by patients with myocardial infarction…" (167)	2	(174) (167)
2.2 Feedback on behaviour	Feedback and monitoring	"Mentors reviewed participants' updated data prior to weekly consultations …. to provide informed, personalised feedback on progress..." (168)	2	(170)(168)
2.6 Biofeedback	Feedback and monitoring	"Before beginning a training session, patients … used the mobile phone to answer a series of questions regarding their present condition, including fatigue, dyspnoea, blood pressure, body mass and medication taken. Patients then transmitted resting ECG data to the monitoring centre. If no contra-indications to training were identified, patients	2	(170)(168)

		were given permission to start the training session." (170)		
5.6 Information about emotional consequences	Natural consequences	"…specific self-help treatments for psychological problems commonly experienced by patients with myocardial infarction….." (167)	2	(166) (167)
6.1 Demonstration of the behaviour	Comparison of behaviour	"A physiotherapist made home visits … in order to develop a training programme that could be performed at home and in the surrounding outdoor area." (171)	2	(173)(171)
8.1 Behavioural practice/rehearsal	Repetition and substitution	"In order to prescribe adequate exercise programmes, a 6 min walk test and a maximal symptom-limited exercise capacity test on bicycle ergometer … was conducted. The main types of exercise recommended were self-paced brisk walking and stationary cycling." (171)	2	(173)(171)
2.7 Feedback on outcome(s) of behaviour	Feedback and monitoring	"…personalised feedback on progress according to goals set." (168)	1	(168)

Table 5a – Baseline characteristics of feasibility study participants

Variable	Group 1 (Control) (SD) (n = 5)	Group 2 (Manual) (SD) (n = 5)	Group 3 (manual + pedometer) (SD) (n = 5)
Sex (M – male, F – female)	4 M 1F	4M 1F	2M 3F
Diagnosis **- TIA** **- Minor stroke**	 1 4	 4 1	 4 1
Mean age (years)	76.2	67.8	63
Mean time (days) -event to enrolment	19.8 (7.09)	22.2 (9.18)	19.6 (3.58)
Level of education - **High school** - **College** - **University**	 3 2 0	 3 2 0	 1 3 1
Employment - **Employed** - **Unemployed** - **Retired**	 1 0 4	 2 1 2	 1 0 4
Multiple deprivation measure (MDM) median (range)*	784 (51 – 863)	413 (250 – 726)	681 (333 – 825)
Family history of cardiovascular disease (<55 years for males, <65 years old for females)	4	3	3
Marital status - **Single** - **Married** - **Divorced**	 1 4 0	 0 5 0	 0 4 1
IPPAQ category **- Inactive** **- Minimally active** **- Health-enhancing physical activity levels (HEPA)**	 2 1 2	 3 1 1	 1 2 2
IPAQ continuous score, mean	1514.6 (1470.06)	870.4 (948.22)	1531.2 (902.5)
IPAQ number of hours sitting/day, mean	6.20 (4.09)	4.80 (1.48)	5.00 (1.00)
Average steps/day in 1st week			8356
Mediterranean diet total score, mean	5.6 (3.13)	6.2 (3.27)	6.0 (2.24)
Mean number of pieces	1.6	2.2	2.0

of vegetables/ day	(1.14)	(1.79)	(1.22)

***Number of participants (n); standard deviation (SD); multiple deprivation measure (MDM) is calculated from the subject's postcode and is a marker of spatial deprivation.**

Table 5b – Baseline characteristics of feasibility study participants

Variable	Group 1 (Control) (SD) (n = 5)	Group 2 (Manual)(SD) (n = 5)	Group 3 (manual + pedometer) (SD) (n = 5)
Mean number of pieces of fruit/day	2.2 (1.92)	2.2 (1.3)	3.4 (0.89)
Systolic blood pressure (mmHg), mean	135.8 (8.41)	136.2 (15.16)	129.4 (15.16)
Diastolic blood pressure (mmHg), mean	76.4 (10.78)	82.8 (13.86)	77.2 (8.14)
Mean resting heart rate (beats per minute)	66.2 (3.03)	65.6 (0.89)	75.0 (9.35)
Average 2 minute walk test performance (meters walked)	109.47 (46.27)	128.82 (29.08)	136.45 (41.54)
Smoking status **- Non-smoker** **- Ex – smoker** **- Current smoker**	 2 3 0	 2 2 1	 3 2 0
Average weekly alcohol intake (units/week)	6.4 (12.12)	5.6 (10.43)	2.8 (3.03)
HADs total score, mean	10.6 (6.54)	10.4 (4.67)	7.00 (4.24)

***Number of participants (n); standard deviation (SD); multiple deprivation measure (MDM) is calculated from the subject's postcode**

and is a marker of spatial deprivation; Hospital Anxiety and Depression questionnaire score (HADs).

Table 5c – Baseline characteristics of feasibility study participants

Variable	Group 1 (Control) (SD) (n = 5)	Group 2 (Manual)(SD) (n = 5)	Group 3 (manual + pedometer) (SD) (n = 5)
HADs Anxiety score, mean	6.00 (4.06)	6.00 (2.12)	5.2 (2.77)
HADs Depression score, mean	4.6 (3.21)	4.4 (3.13)	1.8 (1.92)
EQ5D5L overall index score, mean	0.70 (0.43)	0.85 (0.07)	0.96 (0.04)
EQ5D5L VAS score, mean	66.0 (32.09)	72.0 (17.54)	83.0 (18.23)
Modified Rankin scale **0** **1** **2** **3** **4**	 2 1 1 0 1	 2 1 1 1 0	 4 1 0 0 0
Stages of change for physical activity **1** **2** **3** **4** **5**	 1 0 2 0 2	 1 3 0 0 1	 0 1 1 2 1
Mean height (cm)	171.8 (9.64)	164.9 (4.22)	167.2 (11.86)
Mean weight (kg)	80.62 (10.88)	80.72 (8.14)	79.56 (15.60)
Mean BMI (kg/m^2)	27.26 (2.48)	29.72 (3.22)	28.24 (2.15)

Mean waist circumference (cm)	97.7 (5.74)	99.9 (6.13)	101.2 (11.26)

***Number of participants (n); standard deviation (SD); multiple deprivation measure (MDM) is calculated from the subject's postcode and is a marker of spatial deprivation; Hospital Anxiety and Depression questionnaire score (HADs).**

Table 6 – Post-intervention results for feasibility study participants

Variable	Group 1 (Control) (SD)	Group 2 (Manual) (SD)	Group 3 (manual + pedometer) (SD)
Number of patients in arm	5	5	5
IPAQ continuous score	1093.8 (851.1)	4366.2 (3140.75)	5335.8 (3133.60)
IPAQ number of hours sitting/day	6.3 (3.99)	3.2 (1.30)	3.8 (1.30)
IPAQ category **- Inactive** **- Minimally active** **- Health-enhancing physical activity levels**	 1 4 0	 1 0 4	 0 1 4
Average steps/day in 6th week			9762.8 (3473.45)
Mediterranean diet total score, mean	5.8 (2.49)	8.4 (2.30)	8.0 (1.41)
Mean number of pieces of vegetables/day	1.8 (1.48)	2.4 (0.55)	2.8 (0.84)
Mean number of pieces of fruit/day	2.6 (1.52)	2.8 (1.3)	4.0 (1.41)
Average systolic blood pressure (mmHg)	135.8 (24.83)	128.0 (2.00)	131.0 (12.88)
Average diastolic blood pressure (mmHg)	76.8 (10.01)	74.8 (3.96)	80.4 (11.24)
Average resting heart rate (bpm)	71.6 (8.35)	61.6 (3.36)	73.8 (10.78)
Average 2 minute walk test performance (metres walked)	118.2 (28.15)	149.75 (28.69)	163.38 (23.36)
Mean weekly alcohol intake (units/week)	5.6 (8.41)	1.6 (2.61)	2.4 (2.61)
Average HADs total score	11.0 (5.15)	7.4 (5.50)	3.8 (2.68)
Average HADs Anxiety score	6.2 (3.63)	4.2 (3.49)	3.00 (2.00)
Average HADs Depression score	4.8 (2.39)	3.2 (2.39)	0.8 (1.30)
Mean EQ5D5L overall index score	0.70 (0.37)	0.86 (0.13)	0.96 (0.06)
Mean EQ5D5L VAS score	53.0 (29.71)	86.0 (6.52)	85.8 (17.63)
Modified Rankin scale **0** **1** **2** **3** **4**	 2 1 1 0 1	 2 1 1 1 0	 5 0 0 0 0

Stages of change for physical activity **1** **2** **3** **4** **5**	1 0 2 0 2	0 0 1 3 1	0 0 0 4 1
Mean weight (kg)	80.32 (10.89)	80.06 (8.21)	79.4 (16.45)
Mean BMI (kg/m^2)	27.16 (2.45)	29.49 (3.35)	28.14 (2.18)
Mean waist circumference (cm)	97.7 (5.74)	98.7 (6.53)	100.4 (11.08)

***Number of participants (n); standard deviation (SD); multiple deprivation measure (MDM) is calculated from the subject's postcode and is a marker of spatial deprivation; Hospital Anxiety and Depression questionnaire score (HADs).**

Table 7 – Study Group Baseline and Post-Intervention Measurements (Mean (Standard Deviation (SD)) and categorical values) for the Feasibility Study

Variable	Group 1 (Control) – baseline	Group 1 – post-intervention	Group 2 (Manual) – baseline	Group 2 – post-intervention	Group 3 (Manual + pedometer) – baseline	Group 3 – post-intervention
IPAQ category **- Inactive** **- Minimally active** **- HEPA**	 2 1 2	 1 4 0	 3 1 1	 1 0 4	 1 2 2	 0 1 4
IPAQ continuous score (Mean (SD))	1514.6 (1470.1)	1093.8 (851.1)	870.4 (948.2)	4366.2 (3140.8)	1531.2 (902.5)	5335.8 (3133.6)
IPAQ number of hours sitting/day	6.20 (4.10)	6.3 (4.0)	4.80 (1.5)	3.2 (1.3)	5.00 (1.0)	3.8 (1.3)
Steps/day					8356	9762.8 (3473.5)
Stages of change for physical activity **1** **2** **3** **4** **5**	 1 0 2 0 2	 1 0 2 0 2	 1 3 0 0 1	 0 0 1 3 1	 0 1 1 2 1	 0 0 0 4 1
Mediterranean diet total score	5.6 (3.1)	5.8 (2.5)	6.2 (3.3)	8.4 (2.3)	6.0 (2.2)	8.0 (1.4)

Number of pieces of vegetables/day	1.6 (1.1)	1.8 (1.5)	2.2 (1.8)	2.4 (0.6)	2.0 (1.2)	2.8 (0.8)
Number of pieces of fruit/day	2.2 (1.9)	2.6 (1.5)	2.2 (1.3)	2.8 (1.3)	3.4 (0.9)	4.0 (1.4)
Systolic blood pressure (mmHg)	135.8 (8.4)	135.8 (24.8)	136.2 (15.2)	128 (2.0)	129.4 (15.2)	131.0 (12.9)
Diastolic blood pressure (mmHg)	76.4 (10.8)	76.8 (10.0)	82.8 (13.9)	74.8 (4.0)	77.2 (8.1)	80.4 (11.2)
Resting heart rate (beats per minute)	66.2 (3.0)	71.6 (8.4)	65.6 (0.9)	74.8 (4.0)	75.0 (9.4)	73.8 (10.8)
2 minute walk test performance (metres walked)	109.5 (46.3)	118.2 (28.2)	128.8 (29.1)	149.8 (28.7)	136.5 (41.5)	163.4 (23.4)
Weekly alcohol intake (units/week)	6.4 (12.1)	5.6 (8.4)	5.6 (10.4)	1.6 (2.6)	2.8 (3.0)	2.4 (2.6)
HADs total score	10.6 (6.5)	11.0 (5.2)	10.4 (4.7)	7.4 (5.5)	7.00 (4.2)	3.8 (2.7)
HADs Anxiety score	6.0 (4.1)	6.2 (3.6)	6.0 (2.1)	4.2 (3.5)	5.2 (2.8)	3.0 (2.0)
HADs Depression score	4.6 (3.2)	4.8 (2.4)	4.4 (3.1)	3.2 (2.4)	1.8 (1.9)	0.8 (0.1)
EQ5D5L overall score	0.7 (0.4)	0.7 (0.4)	0.9 (0.1)	1.0 (0.1)	1.0 (0.0)	1.0 (0.1)
EQ5D5L VAS score	66.0 (32.1)	53 (29.7)	72.0 (17.5)	86 (6.5)	83.0 (18.2)	85.8 (17.6)
Weight (kg)	80.6 (10.9)	80.3 (10.9)	80.7 (8.1)	80.1 (8.2)	79.6 (15.6)	79.4 (16.5)
BMI (kg/m^2)	27.3 (2.5)	27.2 (2.5)	29.7 (3.2)	29.5 (3.4)	28.2 (2.2)	28.1 (2.2)
Waist circumference (cm)	97.7 (5.7)	97.7 (5.7)	99.9 (6.1)	98.7 (6.5)	101.2 (11.3)	100.4 (11.1)

***Number of participants (n); standard deviation (SD); multiple deprivation measure (MDM) is calculated from the subject's postcode and is a marker of spatial deprivation; Hospital Anxiety and Depression questionnaire score (HADs).**

Table 8 – Recruitment for Pilot Study

Hospital	Eligible clinic attendees	Number who consented to contact	Total number recruited
Ulster	43	17 (39.5%)	16 (94.1%)
Antrim Area	13	6 (46.2%)	4 (66.7%)
Craigavon Area	53	9 (17.0%)	8 (88.9%)
Royal, Belfast	16	12 (75%)	12 (100%)
Total	125	44(35.2%)	40 (90.9%)

Table 9 (a) Baseline Characteristics of Participants in Pilot Study

Variable	Group 1(n=12) (Control)	Group 2 (GP) (n = 14)	Group 3 (SN) (n = 14)
Mean age (years)	69.67 (14.71)	65.71 (12.99)	63.29 (9.60)
Sex (M – male, F – female)	8 M 4 F	9 M 5 F	6 M 8 F
Diagnosis	6 TIA 6 Minor stroke	12 TIA 2 Minor stroke	9 TIA 5 Minor stroke
Mean (SD) $ABCD^2$ score	3.29 (0.95)	3.67 (1.30)	3.63 (1.12)
No. with $ABCD^2$ score ≥4	3	8	6
No. with NIH score for minor strokes 0 1 2	2 2 2	0 0 2	2 2 1
Mean (SD) days: event to study entry	19.25 (8.85)	15.23 (7.76)	16.87 (7.25)
No. (%) living in 50% most SED areas	7 (58.3)	7 (50)	9 (64.3)
Education - High school Apprenticeship College Undergraduate degree Postgraduate degree	9 1 0 2 0	8 0 3 3 0	10 0 0 2 2
Employment – Employed Unemployed Retired	4 0 8	7 1 6	7 2 5
Marital status - Single Married	0 8	2 8	3 9

Divorced	1	0	2
Widowed	3	3	0
Partnership	0	1	0
Smoking status - Never	4	9	6
Current smoker	5	3	3
Ex-smoker	3	2	5
Mean (SD) units of alcohol per week	6.58 (14.16)	6.50 (10.78)	5.93 (8.78)
Mean IPAQ score (SD) (MET/mins/wk)	1287 (1738)	1104 (1883)	1276 (1397)
IPAQ category - Inactive	8	8	5
- Minimally inactive	3	5	7
- HEPA	1	1	2
Mean IPAQ sitting time/day (SD) (mins)	452.5 (229.4)	533.6 (247.0)	520.0 (351.5)
No. sitting for ≥5 hours daily	8	11	10
Mean (SD) steps/day in 1st week		5546 (4127)	6538 (3993)
Mean (SD) steps/day in 4th week		5965 (4217)	7807 (2927)
Mean (SD) steps/day in 9th week		6582 (5035)	6305 (4406)

*n = number of participants; multiple deprivation measure (MDM), calculated from postcode indicates socio-economic status;
Abbreviations: SN=Stroke Nurse; SED=socio-economically disadvantaged; SD=standard deviation; FH=Family History.

Table 9 (b) Baseline Characteristics of Participants in Pilot Study

Variable	Group 1(n=12) (Control)	Group 2 (GP) (n = 14)	Group 3 (SN) (n = 14)
Mean (SD) sedentary mins/day (accel)	1266 (72.18)	1240 (73.83)	1230 (108.1)
Mean (SD) light PA mins/day	36.11 (12.39)	36.75 (14.83)	32.80 (9.68)
Mean (SD) MPA mins/day	137.2 (65.93)	162. 9 (68.76)	176.6 (100.6)
Mean (SD) VPA mins/day	0.39 (0.67)	0.70 (1.56)	0.31 (0.55)
Mean (SD) MVPA mins/day	137.6 (66.21)	163.6 (68.75)	176.9 (100.8)
No. having a home assessment	1	1	0
Mean SBP (SD) mmHg	140.4 (23.67)	137.9 (16.36)	129.4 (19.75)
Mean DBP (SD) mmHg	140.4 (23.67)	88.9 (11.74)	81.00 (14.53)
Mean (SD) resting heart rate (beats/min)	74.25 (14.4)	68.07 (9.64)	75.0 (7.57)
No. with SBP <130 mmHg	4	3	7
Mean (SD) HADs total score	7.50 (3.06)	9.357 (6.77)	13.21 (10.93)
Mean (SD) HADs depression score	3.08 (1.93)	3.21 (2.99)	5.71 (5.31)
Mean (SD) HADs anxiety score	4.42 (2.84)	6.14 (4.52)	7.50 (6.31)
Mean (SD) weight kg	85.19 (20.52)	88.05 (21.43)	76.78 (12.63)
Mean BMI (SD) kg/m^2	28.98 (3.89)	29.75 (6.68)	28.02 (2.95)
No. with BMI ≥ 30 kg/m^2	5	5	4
Mean waist circumference (SD) cms	99.83 (10.56)	104.3 (15.38)	93.92 (10.16)
Mean 2 minute walk test (SD) metres	127.5 (33.09)	143.5 (53.76)	142.2 (38.59)
Mean TUG test (SD) seconds	13.33 (6.45)	12.90 (7.04)	10.50 (5.96)
Mean EQ5D-5L index score (SD)	0.84 (0.12)	0.79 (0.17)	0.67 (0.30)
Mean (SD) Mediterranean diet score	3.08 (1.56)	4.50 (1.79)	3.57 (2.59)
Mean EQ5D-5L VAS score (SD)	65.83 (13.29)	62.86 (21.90)	69.64 (15.99)
Modified Rankin scale - 0	3	8	8

1	8	4	3
2	1	1	2
3	0	0	0
4	0	1	0
5	0	0	1
No. prescribed: - Aspirin	2	7	4
- Clopidogrel	8	7	9
- Statin	8	12	12
- ACE-Inhibitor	2	6	9
- Anti-hypertensive	3	9	8
Stages of change (No.) - 1	3	4	4
2	2	4	1
3	1	1	1
4	1	0	0
5	5	5	8

*Multiple deprivation measure (MDM), calculated from postcode indicates socio-economic status

** Family history of CVD (1st degree relatives, males aged <55 years; females <65 years)

Abbreviations: SN=Stroke Nurse; SD=standard deviation; SBP=systolic blood pressure; DBP= diastolic blood pressure; mins=minutes; TUG=Timed Up and Go test; accel = accelerometer; PA=physical activity; MPA=moderate PA; VPA= vigorous PA; MVPA=moderate and vigorous PA.

Table 10a – Study Group Baseline and Post-Intervention Measurements (Mean (Standard Deviation (SD)) and categorical values) for Pilot Study

Variables	Group 1 (Control) – baseline (SD – standard deviation) (n = 12)	Group 1 – post-intervention (SD – standard deviation) (n = 12)	Group 2 (GP Follow-up) – baseline (SD – standard deviation) (n = 14)	Group 2 – post-intervention (SD – standard deviation) (n = 14)	Group 3 (Stroke nurse follow-up) – baseline (SD – standard deviation) (n = 14)	Group 3 – post-intervention (SD – standard deviation) (n = 13)
Sex (M – male, F – female)	8M 4F	8M 4F	9M 5F	9M 5F	7M 7F	7M 6F
Smoking status **- Never** **- Current smoker** **- Ex-smoker**	 4 5 3	 4 3 5	 9 3 2	 9 2 3	 6 3 5	 5 2 6
Mean systolic blood pressure, mmHg	140.4 (23.67)	140.8 (8.03)	137.9 (16.36)	127.6 (9.95)	129.4 (19.75)	130.7 (15.79)
Mean diastolic blood pressure, mmHg	84.17 (12.27)	83.58 (16.59)	88.9 (11.74)	80.50 (8.22)	81.00 (14.53)	82.31 (7.50)
Mean resting heart rate, bpm	74.25 (14.4)	76.92 (16.62)	68.07 (9.64)	68.86 (11.17)	75.0 (7.57)	74.85 (9.00)
Number of patients with a systolic blood	4	1	3	7	7	6

pressure <130mmHg						
Average two minute walk test performance, metres	127.5 (33.09)	126.6 (45.84)	143.5 (53.76)	159.0 (50.27)	142.2 (38.59)	160.4 (37.79)
Average timed up and go test, seconds	13.33 (6.50)	12.19 (7.63)	12.9 (7.04)	9.34 (5.80)	10.50 (5.96)	8.15 (2.79)
Mean HADs total score	7.50 (3.06)	6.67 (5.30)	9.36(6.77)	5.64 (5.93)	13.21 (10.93)	8.77 (9.51)
Mean HADs depression score	3.08 (1.93)	3.75 (2.70)	3.21 (2.99)	2.29 (3.32)	5.71 (5.31)	3.31 (4.07)
Mean HADs anxiety score	4.42 (2.84)	2.92 (3.03)	6.14 (4.52)	3.36 (3.15)	7.50 (6.31)	5.46 (5.74)
Mean EQ5D-5L index score	0.84 (0.12)	0.84 (0.21)	0.79 (0.17)	0.85 (0.24)	0.67 (0.30)	0.86 (0.15)
Mean VAS score from EQ5D-5L	65.83 (13.29)	66.25 (11.70)	62.86 (21.90)	71.79 (14.76)	69.64 (15.99)	76.92 (17.50)
Mean units of alcohol per week	6.58 (14.16)	12.75 (34.07)	6.50 (10.78)	4.29 (6.70)	5.93 (8.78)	6.39 (9.45)
Mean weight, kg	85.19 (20.52)	85.83 (21.12)	88.05 (21.43)	86.45 (20.43)	76.78 (12.63)	75.73 (13.26)
Mean BMI, kg/m^2	28.98 (3.89)	29.2 (4.35)	29.75 (6.68)	29.20 (6.28)	28.02 (2.95)	27.72 (3.25)
Mean waist circumference, cms	99.83 (10.56)	102.8 (11.43)	104.3 (15.38)	102.8 (13.98)	93.92 (10.16)	93.63 (10.52)
Modified Rankin						

scale	3	3	8	9	8	7
0	8	7	4	3	3	4
1	1	2	1	2	2	1
2	0	0	0	0	0	0
3	0	0	1	0	0	0
4	0	0	0	0	1	1
5						

Table 10b – Study Group Baseline and Post-Intervention Measurements (Mean (Standard Deviation (SD)) and categorical values) for Pilot Study

Variables	Group 1 (Control) – baseline (SD – standard deviation) (n = 12)	Group 1 – post-intervention (SD – standard deviation) (n = 12)	Group 2 (GP Follow-up) – baseline (SD – standard deviation) (n = 14)	Group 2 – post-intervention (SD – standard deviation) (n = 14)	Group 3 (Stroke nurse follow-up) – baseline (SD – standard deviation) (n = 14)	Group 3 – post-intervention (SD – standard deviation) (n = 13)
Number of patients on: **Aspirin** **Clopidogrel** **Statin** **ACE-Inhibitor**	 2 8 8 2	 2 9 8 2	 7 7 12 6	 7 7 12 6	 4 9 12 9	 5 7 11 6
Mean IPAQ score (MET/minutes/week)	1287 (1738)	2534 (4055)	1104 (1883)	4060 (4865)	1276 (1397)	6787 (13047)
IPAQ category **- Inactive** **- Minimally inactive** **- HEPA**	 8 3 1	 7 3 2	 8 5 1	 3 5 6	 5 7 2	 3 4 6
IPAQ Mean sitting time per day (minutes)	452.5 (229.4)	390.0 (223.8)	533.6 (247.0)	312.9 (156.4)	520.0 (351.5)	378.5 (347.6)
Number of						

participants sitting for 5 or more hours	8	8	11	8	10	7
Average steps/day at 12 wks				6710 (4585)		8423 (4686)
Average sedentary time/day (mins/day) from accel	1266 (72.18)	1266 (90.02)	1240 (73.83)	1210 (110.6)	1230 (108.1)	1236 (98.50)
Average light PA time/day (mins/day) from accel	36.11 (12.39)	36.57 (14.22)	36.75 (14.83)	40.01 (17.30)	32.80 (9.68)	33.03 (8.92)
Average VPA time/day (mins/day) from accel	0.39 (0.67)	0.31 (0.64)	0.70 (1.56)	0.63 (1.51)	0.32 (0.55)	0.20 (0.32)
Average MVPA time/day (mins/day) from accel	137.6 (66.21)	137.1 (79.14)	163.6 (68.75)	190.2 (103.9)	176.9 (100.8)	170.5 (93.29)
Mean Mediterranean diet questionnaire score	3.08 (1.56)	3.46 (1.70)	4.50 (1.79)	7.64 (2.06)	3.57 (2.59)	6.92 (2.78)
Stages of change **1** **2** **3**	 3 2 1	 3 1 3	 4 4 1	 2 2 1	 4 1 1	 3 1 0

4 **5**	1 5	1 4	0 5	2 7	0 8	0 9
Number of times attended the **- GP** **- Practice nurse** **- Hospital outpatient appts** **- A&E dept** **- Admitted to hospital**		 14 14 7 2 1		 15 12 6 1 1		 15 9 6 0 1
Total number of health contacts		38		35		31
Mean number of health contacts over the study		2.67 (1.78)		2.07 (1.39)		2.39 (2.10)

**** Family history of CVD (1st degree relatives, males aged <55 years; females <65 years)**
Abbreviations: SN=Stroke Nurse; SD=standard deviation; SBP=systolic blood pressure; DBP= diastolic blood pressure; mins=minutes; TUG=Timed Up and Go test; accel = accelerometer; PA=physical activity; MPA=moderate PA; VPA= vigorous PA; MVPA=moderate and vigorous PA.

Table 11a – Study Group Baseline and Post-Intervention Measurements (Mean (Standard Deviation (SD)) and categorical values) with ANCOVA analysis for Pilot Study (statistical significance p<0.05)

Variable	Group	Baseline mean (SD – standard deviation)	Post intervention mean (SD – standard deviation)	Mean difference at follow-up (adjusting for baseline)	P-value (ANCOVA)
Systolic blood pressure(mmHg)	**Control (Group 1)**	140.4 (23.67)	140.8 (8.03)	Reference category	
	GP (Group 2)	137.9 (16.36)	127.6 (9.95)	-12.63 (-21.28, -3.98)	**0.005**
	Nurse (Group 3)	129.4 (9.75)	130.7 (15.79)	-7.44 (-16.45, 1.57)	0.103
Diastolic blood pressure (mmHg)	**Group 1**	84.17 (12.27)	83.58 (16.59)	Reference category	
	Group 2	88.9 (11.74)	80.50 (8.22)	-5.03 (-12.79, 2.721)	0.196
	Group 3	81.00 (14.53)	82.31 (7.50)	-0.29 (-8.12, 7.55)	0.941
Average 2 minute walk test	**Group 1**	127.5 (33.09)	126.6 (45.84)	Reference category	

(metres walked)					
	Group 2	143.5 (53.76)	159.0 (50.27)	18.16 (-0.09, 36.41)	0.051
	Group 3	142.2 (38.59)	160.4 (37.79)	21.27 (2.40, 40.14)	**0.028**
Timed up and go test (TUGT) (seconds)	**Group 1**	13.33 (6.50)	12.19 (7.63)	Reference category	
	Group 2	12.9 (7.04)	9.34 (5.80)	-2.54 (-5.17, 0.10)	0.059
	Group 3	10.50 (5.96)	8.15 (2.79)	-2.11 (-4.84, 0.67)	0.132
HADs total score	**Group 1**	7.50 (3.06)	6.67 (5.30)	Reference category	
	Group 2	9.36(6.77)	5.64 (5.93)	-2.51 (-5.55, 0.54)	0.104
	Group 3	13.21 (10.93)	8.77 (9.51)	-3.15 (-6.42, 0.13)	0.059
EQ5D-5L VAS score	**Group 1**	65.83 (13.29)	66.25 (11.70)	Reference category	
	Group 2	62.86 (21.90)	71.79 (14.76)	6.39 (-4.99, 17.77)	0.262
	Group 3	69.64 (15.99)	76.92 (17.50)	9.81 (-1.78, 21.39)	0.094

Weight (kg)	**Group 1**	85.19 (20.52)	85.83 (21.12)	Reference category	
	Group 2	88.05 (21.43)	86.45 (20.43)	-2.20 (-4.02, -0.38)	**0.019**
	Group 3	76.78 (12.63)	75.73 (13.26)	-1.22 (-3.14, 0.71)	0.207

Table 11b – Study Group Baseline and Post-Intervention Measurements (Mean (Standard Deviation (SD)) and categorical values) with ANCOVA analysis for Pilot Study (statistical significance p<0.05)

Variable	Group	Baseline mean (SD – standard deviation)	Post intervention mean (SD – standard deviation)	Mean difference at follow-up (adjusting for baseline)	P-value (ANCOVA)
Waist circumference (cms)	**Group 1**	99.83 (10.56)	102.8 (11.43)	Reference category	
	Group 2	104.3 (15.38)	102.8 (13.98)	-4.20 (-7.00, -1.41)	**0.004**
	Group 3	93.92 (10.16)	93.63 (10.52)	-2.82 (-5.76, 0.11)	0.059
IPAQ score (MET/minutes/week)	**Group 1**	1287 (1738)	2534 (4055)	Reference category	
	Group 2	1104 (1883)	4060 (4865)	1831 (-4565, 8226)	0.565
	Group 3	1276 (1397)	6787 (13047)	4346 (-2156, 10848)	0.184
IPAQ mean sitting time/day (mins/day)	**Group 1**	452.5 (229.4)	390.0 (223.8)	Reference value	

	Group 2	533.6 (247.0)	312.9 (156.4)	-125.8 (-282.1, 30.50)	0.111
	Group 3	520.0 (351.5)	378.5 (347.6)	-59.45 (-218.4, 99.53)	0.453
Mediterranean Diet Questionnaire score	**Group 1**	3.08 (1.56)	3.46 (1.70)	Reference category	
	Group 2	4.50 (1.79)	7.64 (2.06)	3.56 (1.90, 5.22)	**0.000**
	Group 3	3.57 (2.59)	6.92 (2.78)	3.37 (1.73, 5.02)	**0.000**
Resting heart rate (bpm)	**Group 1**	74.25 (14.4)	76.92 (16.62)	Reference category	
	Group 2	68.07 (9.64)	68.86 (11.17)	-1.83 (-7.30, 3.64)	0.501
	Group 3	75.0 (7.57)	74.85 (9.00)	-1.74 (-7.15, 3.66)	0.517
Average sedentary time/day (mins/day) from accelerometer	**Group 1**	1266 (72.18)	1266 (90.02)	Reference category	
	Group 2	1240 (73.83)	1210 (110.6)	-32.51 (-83.20, 18.17)	0.201
	Group 3	1230 (108.1)	1236 (98.50)	7.55 (-46.76, 61.86)	0.779
Average light PA time/day (mins/day)	**Group 1**	36.11 (12.39)	36.57 (14.22)	Reference category	

from accelerometer					
	Group 2	36.75 (14.83)	40.01 (17.30)	2.89 (-4.52, 10.30)	0.433
	Group 3	32.80 (9.68)	33.03 (8.92)	-1.65 (-9.54, 6.23)	0.672
Average MPA time/day (mins/day) from accelerometer	**Group 1**	137.2 (65.93)	136.8 (79.03)	Reference category	
	Group 2	162. 9 (68.76)	189.5 (103.8)	29.52 (-16.94, 75.98)	0.205
	Group 3	176.6 (100.6)	170.3 (93.15)	-6.11 (-56.12, 43.90)	0.805
Average VPA time/day (mins/day) from accelerometer	**Group 1**	0.39 (0.67)	0.31 (0.64)	Reference category	
	Group 2	0.70 (1.56)	0.63 (1.51)	0.08 (-0.38, 0.53)	0.735
	Group 3	0.32 (0.55)	0.20 (0.32)	-0.03 (-0.51, 0.44)	0.884
Average MVPA time/day (mins/day) from accelerometer	**Group 1**	137.6 (66.21)	137.1 (79.14)	Reference category	
	Group 2	163.6 (68.75)	190.2 (103.9)	29.57 (-16.93, 76.08)	0.205

	Group 3	176.9 (100.8)	170.5 (93.29)	-6.07 (-56.10, 43.97)	0.807

***PA=physical activity; MPA=moderate PA; VPA= vigorous PA; MVPA=moderate and vigorous PA.**

Appendix I

Database(s): Ovid MEDLINE(R) 1946 to October Week 5 2014

1) Ischemic Attack, Transient

2) TIA*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

3) "transient isch?emic attack*".mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

4) stroke/ or brain infarction/ or brain stem infarctions/ or lateral medullary syndrome/ or cerebral infarction/ or infarction, anterior cerebral artery/ or infarction, middle cerebral artery/ or infarction, posterior cerebral artery/ or stroke, lacunar/

5) (minor adj5 stroke*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

6) 1 or 2 or 3 or 4 or 5

7) rehabilitation/ or "activities of daily living"/ or animal assisted therapy/ or art therapy/ or bibliotherapy/ or "correction of hearing impairment"/ or dance therapy/ or early ambulation/ or exercise therapy/ or music therapy/ or myofunctional therapy/ or occupational therapy/ or recreation therapy/ or "rehabilitation of speech and language disorders"/ or rehabilitation, vocational/

8) rehabilitat*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

9) 7 or 8

10) 6 and 9

11) exp Community Health Services

12) ("community based" or "in the community").mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

13) home care services/ or home health nursing/ or home nursing/

14) "home based".mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier

15) 11 or 12 or 13 or 14

16) 10 and 15

17) ("within 90 days" or "within ninety days" or early).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word,

protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

18) 16 and 17

For studies assessing just cardiac rehabilitation following an initial TIA or 'minor' stroke:

19) exp Rehabilitation/

20) exp Cardiology/

21) 19 and 20

22) 21 and "cardiac rehabilitat*".mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

23) 18 and 22 24) 6 and 23 25) 6 and 22

Appendix II

Author, title

Methods, Participants

Interventions

Outcomes

Notes

Risk of bias

Random sequence generation (selection bias)

Allocation concealment (selection bias)

Blinding of participants and personnel (performance bias)

Blinding of outcome assessment (detection bias)

Incomplete outcome data (attrition bias)

Selective reporting (reporting bias)

Other bias

Appendix III

Database(s): Ovid MEDLINE(R) 1946 to June 2015

1) Myocardial infarction, ‘heart attack’

2) Angina

3) Angioplasty

4) Heart failure

5) Cardiac rehabilitation/rehab

6) 1 or 2 or 3 or 4 or 5

7) rehabilitation/ or "activities of daily living"/ or animal assisted therapy/ or art therapy/ or bibliotherapy/ or "correction of hearing impairment"/ or dance therapy/ or early ambulation/ or exercise therapy/ or music therapy/ or myofunctional therapy/ or

occupational therapy/ or recreation therapy/ or "rehabilitation of speech and language disorders"/ or rehabilitation, vocational/

8) rehabilitat*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

9) 7 or 8

10) 6 and 9

11) exp Community Health Services

12) ("community based" or "in the community").mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

13) home care services/ or home health nursing/ or home nursing/

14) "home based".mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier

15) 11 or 12 or 13 or 14

16) 10 and 15

17) 16 limited to 2005 - 2015

Appendix IV

Appendix V - General questions for patients/health professionals:

1) What do you think about the general level of information included within the booklet – too much/too little?
2) What do you think of the exercise programme? Would you be able to do this within your own home? Is it hard enough?
3) Is there anything in particular which would worry you about exercising or asking people to exercise after a TIA/stroke?
4) What do you think of the length of the booklet? Is it too short? Is it too long?
5) What do you think of the layout of the booklet? Does it need more colour, pictures, different font size, etc?
6) Would you like a patient story within the book – detailing their thoughts/emotions after being diagnosed with a TIA/minor stroke?
7) Are there any risk factors which haven't been covered, which you would like included? Are there any risk factors which you would like more information on – or less to be given?

Appendix VI

Focus group topic guide:

Impact of the diagnosis/illness on the patient:

1) After the diagnosis, what was your biggest problem, e.g. fatigue?
2) How did the diagnosis affect your life?

Views on the manual:

3) What do you think of the manual?
4) What do you think about the general level of information included within the booklet – too much/too little?
5) What do you think of the length of the booklet? Is it too short? Is it too long?
6) What do you think of the layout of the booklet? Does it need more colour, pictures, different font size, etc?
7) Would you like a patient story within the book – detailing their thoughts/emotions after being diagnosed with a TIA/minor stroke?

8) Are there any risk factors which haven't been covered, which you would like included? Are there any risk factors on which you would like more information to be given – or less?
9) Did family members read the manual? What did they think? Anything which you particularly enjoyed about the manual?
10) Anything you would improve about the manual?

Exercise programme within the manual:

11) Is there anything in particular which would worry you about exercising or asking people to exercise after a TIA/stroke?
12) What do you think of the exercise programme? Would you be able to do this within your own home? Is it hard enough?

Study duration and future goals:

13) What goals/aims are important to you now that you have been diagnosed and are on the path to recovery?
14) What did you think about the duration of the study follow-up? Longer/shorter?

Review of FitBit v pedometer:

15) What are your views on the pedometer?
16) How did people find using the FitBit compared to the pedometer? What did you prefer/ why?
17) What made you stop using the FitBit?

Research assessments and exercise treadmill test:

18) What did people think about how they were invited and then recruited into the research study?
19) What did people think about the research assessments?
20) What did people think about the amount of time involved in the research assessments?
21) Why did people refuse to consent to the treadmill/bicycle exercise test?

Appendix VII

Appendix VIII

Study: SPRITE – A Pilot Study

Patient research code:

First name:

Patient telephone contact number:

Telephone follow-up review at end of week 1:

Date and time of call:

Duration of call (minutes and seconds):

Throughout the telephone calls, adopt a **motivational interviewing approach**. Try to **avoid conflict with the participants** – the participants will decide if they wish to tackle a particular issue. Your role is to gently challenge the participant and provide appropriate health advice to your level of training.

Welcome the patient and thank them for taking part in the research study.

At each telephone conversation, ask the patient:

1) Are there any particular questions which they would like answered?

2) Every patient has a pedometer, review their average step counts for the previous week and write down the daily step counts and average achieved for the last week. **Encourage participants to keep a daily diary of their step-counts**.

3) What are their goals which they wrote down at the start of the manual/programme? Are they achieving them? If not, why not? What can they do differently to achieve them? Is there anything which health professionals can do to help them? Signpost them to appropriate support, e.g. smoking cessation clinics, local pharmacy, GP surgery, local charities, etc depending on the patient needs.

If they are achieving their goals, are there any new goals which they would like to achieve? Get them to write these down as well as an action plan on how to achieve them. Action plan examples are included in the Introduction of the manual.

4) Finish the conversation by reviewing the next section of the manual with them.

5) Any other questions which they would like answered?

If you have any questions about this or anything which you are not sure about, please contact **Dr Heron** on the above number (**07808774292**) to clarify this.

Telephone follow-up review at end of week 4:

Date and time of call:

Duration of call (minutes and seconds):

1) Are there any particular questions which they would like answered?

2) Every patient has a pedometer, review their average step counts for the previous week and write down the daily step counts and average achieved for the last week. **Encourage participants to keep a daily diary of their step-counts**.

3) What are their goals which they wrote down at the start of the manual/programme? Are they achieving them? If not, why not? What can they do differently to achieve them? Is there anything which health professionals can do to help them? Sign post them to appropriate support, e.g. smoking cessation clinics, local pharmacy, GP surgery, local charities, etc depending on the patient's needs.

If they are achieving their goals, are there any new goals which they would like to achieve? Get them to write these down as well as an action plan on how to achieve them. Action plan examples are included in the Introduction of the manual.

4) Finish the conversation by reviewing the next section of the manual with them.

5) Any other questions which they would like answered?

At the end of the first 6 weeks, encourage the person to continue to read the manual intermittently for the rest of the study duration (12 weeks) and to continue to set themselves step-count targets to achieve each week. Again, encourage the use of a **step-diary** or **physical activity diary**.

If you have any questions about this or anything which you are not sure about, please contact **Dr Neil Heron** on the above number (**07808774292**) to clarify this.

Telephone follow-up review at end of week 9:

Date and time of call:

Duration of call (minutes and seconds):

1) Are there any particular questions which they would like answered?

2) Every patient has a pedometer, review their average step counts for the previous week and write down the daily step counts and average achieved for the last week. **Encourage participants to keep a daily diary of their step-counts**.

3) What are their goals which they wrote down at the start of the manual/programme? Are they achieving them? If not, why not? What can they do differently to achieve them? Is there anything which health professionals can do to help them? Sign post them to appropriate support, e.g. smoking cessation clinics, local pharmacy, GP surgery, local charities, etc depending on the patient needs.

If they are achieving their goals, are there any new goals which they would like to achieve? Get them to write these down as well as an action plan about how to achieve them.

4) Finish the conversation by reviewing the next section of the manual with them.
5) Any other questions which they would like answered?

If you have any questions about this or anything which you are not sure about, please contact **Dr Neil Heron** on the above number (**07808774292**) to clarify this.

NB - At the end of the 9 week telephone conversation, please contact Dr Neil Heron on 07808774292 to arrange their final assessment (at 12 weeks). Please advise the patient that Dr Heron will be in contact with them to arrange this final assessment which will take place in the Northern Ireland Clinical Research Facility (NICRF), Level U, Belfast City Hospital.

Appendix IX

End of pilot study questions for patients and stroke nurses, focus group February 2018:

Recruitment:

I'm interested in knowing your views about the recruitment process to the study

- How did you feel about being given information at the TIA clinic and being asked if someone could contact you by phone?
- How did you feel about being contacted by someone you'd not met?
- How did you feel about being asked to come to the research unit in Belfast to take part in the study?
- Would it have made a difference to your response if you could have been seen anywhere else – (eg GP surgery/ local hospital/home?)
- Do you think people might have preferred other ways of being invited to take part, or meeting the researcher?

Views on the manual:

- What do you think of the manual? How often did you use or refer to it? Was there anything you found hard to understand or would want more information on?
- What do you think about the general level of information included within the manual – too much/too little?
- What do you think of the length of the booklet? (short/ long)?
- What do you think of the layout of the booklet? (colour, pictures, font size)?
- What did you think of the patient story?
- Did family members/ friends read the manual? What did they think?
- Anything which you particularly enjoyed or disliked about the manual? Anything you would change in it?
- If an app version of the manual was available, would people use it?

Exercise programme within the manual:

- How do you feel about exercise after having had a TIA/stroke?
- What do you think of the exercise programme in the manual? Could you do this in your own home? Is it challenging?

Use of pedometer:

- What are your views on using the pedometer/ step-count goals with the manual?
- What would you think of using an electronic aid, e.g. Fitbit, app on phone to help you get more active?

Follow-up contact:

- What were your views on the telephone contacts during the study? (number/ frequency/ content (topics covered/ feedback given)/ GP/ nurse?)
- About how much time did each telephone call take up for you?
- Are there other ways of follow-up which you would like to see included, e.g. group meetings, on-line chat rooms?

Research methods:

- What did you think about the tests and measurements that were done as assessments? (comments about the examination/ questionnaires?)
- What did you think about the time involved in the assessments?
- Are there any tests which you would have preferred not to do or would like to see included?
- What do you think would incentivise more people to take part in studies like this?

Dissemination of research findings:

- Who do you think should be told about our study's findings?
- What do you think is the best way to tell people about our findings?

Study duration and future goals:

- What goals/aims are important to you now that you have been diagnosed and are on the path to recovery?
- What did you think about the 12-week study follow-up? Longer/shorter?

Supplementary File 1 – BCTs utilised within the Manual Preface

BCT Label	BCT group	Example of how the BCT was used
2.4 Self-monitoring of outcome(s) of behaviour	2. Feedback and monitoring	"Please remember to visit them (GP/practice nurses) regularly for health advice, e.g. to monitor your BP…"
3.1 Social support (unspecified)	3. Social support	"This manual can also be shared with your family and friends…as well as with your General Practitioner (GP) and practice nurse"
3.2 Social support (practical)	3. Social support	"The facilitator, who will contact you by telephone, will help you go through the book."
5.3 Information about social and environmental	5. Natural consequences	"….giving you information about TIAs, minor strokes, your brain and the impact which your diagnosis can have on your

consequences		life."
9.1 Credible source	9. Comparison of outcomes	"Your facilitator, GP and practice nurse are good sources of health information."
13.2 Framing/Reframing	13. Identity	"This manual contains information about ways you can help yourself to feel good now and remain healthy in the future."

Supplementary File 2 – BCTs utilised within the Manual Introduction

BCT Label	BCT group	Example of how the BCT was used
1.1 Goal setting (behaviour)	1. Goals and planning	"Have realistic goals." Patient encouraged to keep a goal and action plans diary and write this down within the manual.
1.3 Goal setting (outcome)	1. Goals and planning	"Goal – stress (reduction). Plan – I will join a yoga class. I will find out about where there are yoga classes happening and I will sign up to attend a class once a week starting from next week."
1.4 Action planning	1. Goals and planning	"Make an action plan." Patient encouraged to keep a goal and action plans diary and write this down

		within the manual.
1.7 Review outcome goal(s)	1. Goals and planning	“Write a few goals and action plans down for you to try to achieve over the next few weeks. You can discuss how to achieve these with your facilitator or other health professional.”
1.8 Behavioural contract	1. Goals and planning	The goals and action plans diary is agreed with the facilitator.
3.1 Social support (unspecified)	3. Social support	Advice provided about what to do if they suspect they are having another TIA or stroke.
3.2 Social support (practical)	3. Social support	“….try to contact someone who could come and be with you while you are waiting for the ambulance.”
5.1 Information about health consequences	5. Natural consequences	“The fact that you have had a TIA or minor stroke doesn’t mean that your brain is worn out or that you are

		'finished' but should serve as a warning to you that you need to improve your health." "Changing the way you live, such as making small changes to your diet or getting more exercise, can reduce your risk of having another transient ischaemic attack (TIA) or stroke…."
5.6 Information about emotional consequences	5. Natural consequences	"These changes can also make you feel better and more energetic."
11.2 Reduce negative emotions	11. Regulation	"After a TIA or stroke it is common to notice unusual feelings in your body much more than you did before. It is important not to get too worried about this. Worrying and thinking about these

		sensations can often make them seem worse.”
13.2 Framing/ reframing	13. Identity	“The good news is that it’s well on the way to recovery already.”
15.1 Verbal persuasion about capability	15. Self-belief	“Things to remember: - The brain has miraculous powers of recovery. - It is one of the strongest and most adaptable organs in your body. - It is also capable of doing much more work than most of us ever need.” “People who have realistic goals and plan changes have greater success in changing the way they live.”

Supplementary File 3 – BCTs utilised within Section 1 - Smoking

BCT Label	BCT group	Example of how the BCT was used
1.1 Goal setting (behaviour)	1. Goals and planning	"Weigh these up for yourself and decide whether you are ready to quit."
1.2 Problem solving	1. Goals and planning	"Identify situations that will be difficult and plan how you'll cope…"
1.4 Action planning	1. Goals and planning	"Try taking chewing gum or something healthy rather than a cigarette." "Some people say that smoking is good for them because it helps them to relax. If this is the case for you, think of other ways to relax. Perhaps going for a walk, instead of having a cigarette, might make you feel good?"
3.1 Social	3. Social	"Perhaps a friend or someone in your

support (unspecified)	support	family wants to stop too?" "For those experiencing specific difficulties and challenges, there is specific help available in the community and your facilitator can help identify this."
4.1 Instruction on how to perform the behaviour	4. Shaping knowledge	"If you enjoy a cigarette after a meal, clean your teeth after eating if possible."
4.2 Information about Antecedents	4. Shaping knowledge	"Stick with it….. - even though you may have withdrawal symptoms once you stop smoking. These should disappear within a week or two. - Don't give in to cravings – these

		usually only last a few minutes and then pass.”
5.1 Information about health consequences	5. Natural consequences	“It is never too late to stop smoking and the benefits begin as soon as you give up: - Within days, your blood is less likely to clot. - Within 5 years, the risk of a heart attack falls to half that of a smoker. Within 10 years, you will have about the same risk of heart and brain disease as someone who has never smoked.”
8.2 Behaviour substitution	8. Repetition and substitution	“If you normally have a cigarette first thing in the morning, get up and have a shower instead.”
8.4 Habit reversal	8. Repetition and	“If you like a cigarette with tea or coffee, try changing your drink to water

	substitution	or a fruit juice."
9.2 Pros and cons	9. Comparison of outcomes	"First, think about the reasons you like smoking and the reasons you would like to quit smoking."
10.3 Non-specific reward 10.6 Non-specific incentive 10.7 Self-incentive 10.9 Self-reward	10. Reward and threat	"Be nice to yourself: - Reward yourself for staying off cigarettes, even for one day. - Save the money you are not spending on cigarettes to buy yourself something nice."
11.1 Pharmacologic-al support	11. Regulation	"There are treatments available that can at least double your chances of quitting…"
12.1	12.	"If you like to smoke when chatting on

Restructuring the physical environment	Antecedents	the phone, move the ashtray.”

Supplementary File 4 – BCTs utilised within Section 2 – Physical Activity

BCT Label	BCT group	Example of how the BCT was used
1.1 Goal setting (behaviour)	1. Goals and planning	"Your aim is to build up to 30 minutes of moderate activity every day and reduce the amount of time you spend being inactive." "To help guide the intensity of your physical activity/exercise: moderate intensity activity is when you're working hard enough to raise your heart rate and break into a sweat."
1.2 Problem solving	1. Goals and planning	"Finding a way of being active can sometimes be hard, so here are some tips on how to make it easier for

		yourself: - Choose an activity you enjoy! - Listen to music whilst you exercise. - Try and find activities that fit in with your lifestyle and that you can do on most days of the week." "Give the car a rest – walk or cycle to the shops, church or work."
2.3 Self-monitoring of behaviour	2. Feedback and monitoring	"A general target to aim for is about 7,500 steps/day although some people will manage more than this…" "You will be able to talk but unable to sing the words to a song (the 'talk-sing' test)."

		"Physical activity and exercise record". "Please continue writing at the end of the manual, use a separate diary or an app on your phone to record your activity levels."
3.1 Social support (unspecified)	3. Social support	"….set your own personal target after talking to the facilitator." "Sexual counselling".
3.2 Social support (practical)	3. Social support	"Chest Heart and Stroke (NI) organise exercise classes (called Post Rehab Exercise Programme – PREP) for patients and can be accessed directly

		through the Association.”
3.3 Social support (emotional)	3. Social support	“Having company can make exercising more enjoyable.” “Discuss the problem with your partner so that they know that they aren’t putting you off.”
4.1 Instruction on how to perform the behaviour	4. Shaping knowledge	Written explanation of 5 exercises to try at home.
6.1 Demonstration of the behaviour	6. Comparison of behaviour	The home exercise programme is illustrated to the reader through appropriate diagrams.
7.1 Prompts/cues	7. Associations	For being physically active: “- Keep your walking shoes near the door.

		- Keep your golf clubs or swim suit in the boot of the car."
8.1 Behavioural practice/ rehearsal	8. Repetition and substitution	"Add activity to your daily routine – begin with three 10-minute walks spread throughout your day, for example."
9.1 Credible source	9. Comparison of outcomes	"Some GPs can also refer you to your local council gyms through local initiatives, e.g. Healthwise scheme."
11.2 Reduce negative emotions	11. Regulation	"This often leads to avoiding sex or not enjoying it when it does happen. In fact, it seems to be very rare for a person to have a TIA or stroke after having sex."
12.5 Adding objects to the environment	12. Antecedents	"A pedometer…"
13.2 Framing/ reframing	13. Identity	"It is important to realise that sex is no different from any other kind of

		exercise. It does not put a special kind of strain on your brain.”

Supplementary File 5 – BCTs utilised within Section 3 – Healthy Eating and Alcohol

BCT Label	BCT group	Example of how the BCT was used
1.1 Goal setting (behaviours)	1. Goals and planning	"Safe limits of alcohol intake: 1) 14 units per week for both men and women; 2) spread your alcohol intake evenly throughout the week; 3) maximum of 2-3 units per day." - " I will use only semi-skimmed milk. - I won't have second helping. - I will eat a healthy breakfast every morning like Weetabix or porridge…."

1.3 Goal setting (outcome)	1. Goals and planning	"Aim to lose weight slowly. Short-term or quick-fix diets are not good – you need to make changes you can keep to long-term."
1.4 Action planning	1. Goal and planning	"Recommendations to adopt a Mediterranean-style diet:…." "Make out a shopiing list with all the healthy foods you plan to buy, then take it with you to the shop."
1.5 Review	1. Goal and	"Keep a Food Diary….You might be

behaviour goal(s)	planning	surprised to see what your Food Diary looks like after one week! Try writing this down and discussing it with the facilitator."
2.3 Self-monitoring of behaviour	2. Feedback and monitoring	"Set Targets for Yourself…"
4.1 Instruction on how to perform the behaviour	4. Shaping knowledge	"There are four main messages when eating for a healthy brain and heart: - Eat less fat – especially saturated fat. - Eat more fibre – fruits, vegetables, cereals. - Eat less salt. - Eat less sugar." "Here are some helpful tips to make it

		easier for you to switch to healthier eating choices – and to enjoy them!”
5.1 Information about health consequences	5. Natural consequences	“A healthy Mediterranean diet can help prevent further brain disease, as well as other diseases such as heart attacks, by: 1. Lowering cholesterol in the blood vessels around your heart. 2. Controlling your weight, which affects your blood pressure. Supplying you with vitamins and antioxidants, which help to keep your blood vessels in good shape.”
5.6 Information about emotional consequences	5. Natural consequences	“After a few weeks you may find that you can enjoy yourself just as much on a lot less alcohol.”

6.2 Social comparison	6. Comparison of behaviour	"A Patient's Story" A patient details their experience of suffering a TIA.
8.1 Behavioural practice/ rehearsal	8. Repetition and substitution	"Eat more fruit and vegetables – aim for minimum 5 portions/day….oily fish (2/3 times/week)."
8.2 Behaviour substitution	8. Repetition and substitution	"Switch to olive oil and rapeseed oil instead of lard or other vegetable oils - Switch to olive oil spreads instead of butter or margarine". "….try making every other drink a low-alcohol drink."

		"Try half-fat or low-fat dairy products…."
9.1 Credible source	9. Comparison of outcomes	"A Patient's Story" A patient details their experience of suffering a TIA.
10.3 Non-specific reward	10. Reward and threat	"Enjoy a treat once a week as a reward."

Supplementary File 6 – BCTs utilised within Section 4 – Stress and Fatigue

BCT Label	BCT group	Example of how the BCT was used
1.1 Goal setting (behaviour)	Goals and planning	"- Keep active – a healthy body helps keep a healthy mind." "…take adequate rest periods during the day…."
1.2 Problem solving	1. Goals and planning	"The way we think about a situation is part of what makes it stressful. It's not always the situation itself that matters most, but our response to it." "Practical Ways to Help you Control your Stress"
2.3 Self-monitoring of	2. Feedback and monitoring	"…keeping a diary of your activities can help with this."

behaviour		
3.1 Social support (unspecified)	3. Social support	"If you are finding it difficult to sleep, discuss this with your GP or another health professional."
3.2 Social support (practical)	3. Social support	"Speak with your GP or healthcare professional who can suggest some treatments, e.g. ….antidepressant medication"
3.3 Social support (emotional)	3. Social support	"Speak with your GP or healthcare professional who can suggest some treatments, e.g. counselling…"
4.2 Information about Antecedents	4. Shaping knowledge	"two people might experience the same stressful situation in two different ways: One might say it makes them feel helpless against an impossible barrier, as in a nightmare or a trap, with pressure from both sides – like being the meat in

		a sandwich. Another person might view the same situation as an obstacle which can be overcome – an exciting opportunity or a challenge, like a successful juggler.”
5.1 Information about health consequences	5. Natural consequences	“Long periods of stress can lead to: - High blood pressure - Muscle tension and backache…”
5.3 Information about social and environmental consequences	5. Natural consequences	“Without stress and adrenaline, we might never get anything done!”
5.6 Information about emotional consequences	5. Natural consequences	“Long periods of stress can lead to: - Frustration, irritability and anxiety…”
9.1 Credible	9. Comparison	“..speak to your GP…”

source	of outcomes	
11.2 Reduce negative emotions	11. Regulation	“Try not to be a perfectionist in everything.”

Supplementary File 7 – BCTs utilised within Section 5 - Medication

BCT Label	BCT group	Example of how the BCT was used
1.2 Problem solving	1. Goals and planning	"You may find it useful to make a list of all the medicine you have to take, at which time and connect it with something you usually do at that time – like your morning wash, eating lunch, getting changed after work or going to bed."
1.4 Action planning	1. Goals and planning	"You may find it useful to make a list of all the medicine you have to take, at which time and connect it with something you usually do at that time – like your morning wash, eating lunch, getting changed after work or going to bed."
7.1 Prompts/cues	7. Associations	"You may find it useful to make a list of all the medicine you have to take, at

		which time and connect it with something you usually do at that time – like your morning wash, eating lunch, getting changed after work or going to bed.”
8.1 Behavioural practice/ rehearsal	8. Repetition and substitution	“If you always take them at these times it will soon become a habit and you are less likely to forget.”
8.3 Habit formation	8. Repetition and substitution	“If you always take them at these times it will soon become a habit and you are less likely to forget.”
9.1 Credible source	9. Comparison of outcomes	“…ask your doctor.”
11.1 Pharmacologic-al support	11. Regulation	“Medication to Help your Brain”.

Supplementary File 8 – BCTs utilised within Section 6 – Community Support

BCT Label	BCT group	Example of how the BCT was used
3.2 Social support (practical)	3. Social support	"A friend or family member may join you, for example, in starting an exercise programme or indeed you may quit smoking together."
9.1 Credible source	9. Comparison of outcomes	"Your facilitator, doctor or practice nurse will help you to identify organisations and services in your area that can help you in whatever positive lifestyle changes you choose to make."

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